AUGUST, 1950

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

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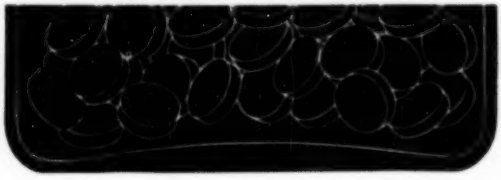

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(INCORPORATING THE AMERICAN JOURNAL OF GASTROENTEROLOGY)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

VOLUME 17 AUGUST, 1950 NUMBER 8

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Owned and published monthly by the National Gastroenterological Association, Inc. Editorial Office: 146 Central Park West, New York 23, N. Y. Business Office: 1819 Broadway, New York 23, N. Y. Subscription rate, U. S., Pan-American Union: One year $5.00, two years $9.00 (foreign $7.00, $13.00) Single copy: $.50. *Reentered as second class matter, February 24, 1947, at the Post Office at New York, N. Y., under the act of March 3, 1879.*

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OFFICIAL PUBLICATION

of the

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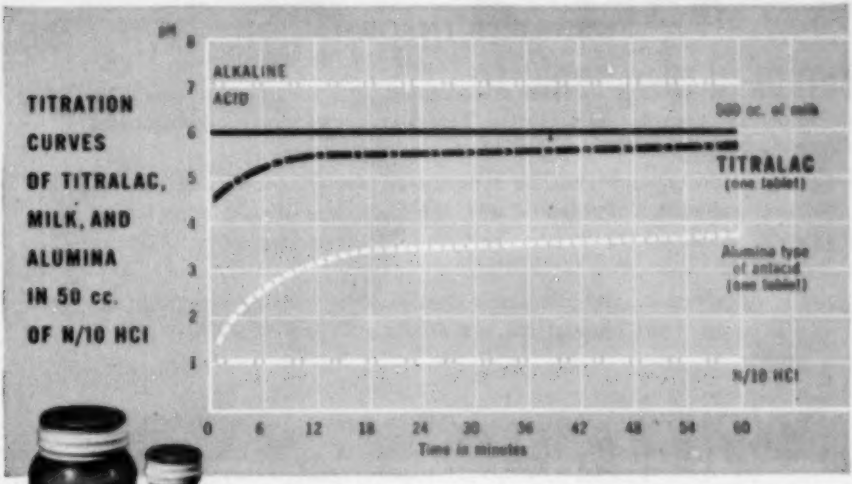

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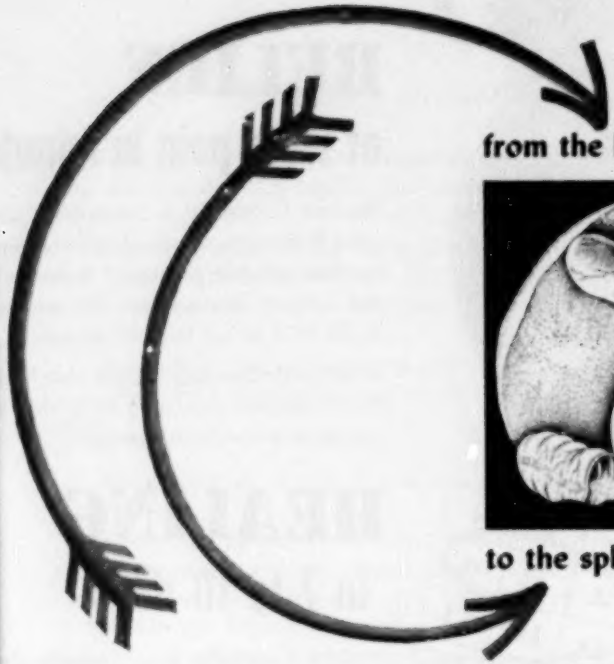

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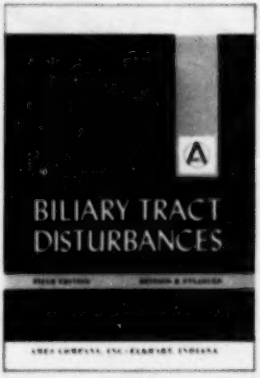

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The Review of Gastroenterology

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A monthly journal of Gastroenterology, Proctology and Allied Subjects

Volume 17 AUGUST, 1950 Number 8

LIVER TRAUMA*†

GEORGE W. PAPEN, M.D., F.A.C.S.**

and

STANLEY MIKAL, M.D.††

Boston, Mass.

Much has been written in relation to functional disease of the liver, methods of diagnosis and efforts to relieve impaired liver function due either to disease of the liver itself or disease changes in the liver subsequent to infection causing general systemic pathological changes. Inasmuch as the liver is such an integral part of the proper functioning of the gastrointestinal system the question of liver trauma and its attendant complications merits consideration in the overall discussion of gastrointestinal diseases. The problem of conserving life in liver trauma is no less important than the problem of relieving organic or functional disease of the liver. Recent use of absorbable hemostatics such as oxidized cellulose (oxycel) and gelatin sponge (gelfoam) has been a great addition to our armamentaria in the progress of surgery of the liver.

Historical Review

In 1888 Langenbuch[1], with mass ligatures, controlled severe liver hemorrhage following partial resection.

Kousnetzoff and Penski[2], in 1896, devised a special needle for liver suture. The needle was large, curved, wedge-shaped and blunt tipped. It was passed through the liver with a continuous suture. The suture was subsequently cut up into single mattress sutures and tied. If any large vessels continued to bleed from the cut liver surface they were circumstitched and ligated.

Ceccherelli and Bianchi[3], in 1894, reported on the use of decalcified bone plates in controlling hemorrhage from the liver. They placed the bone plates on the upper and lower surfaces of the liver and secured them with through-and-through sutures. In a similar manner, Payer used magnesium plates, and Segale ivory rods[4].

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*Read before the Fourteenth Annual Convention of the National Gastroenterological Association, Boston, Mass., 24, 25, 26 October 1949.

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Terrier and Auvray[5], in 1898, used a continuous-chain-suture technic for hepatic hemostasis with good results.

In 1902 Beck[6] employed a Nelaton rubber catheter for elastic compression around the cut surface of the liver, together with iodoform gauze as a tampon. The catheter and gauze were brought out through the abdominal wound and removed in four to six days. Later, in the same year, he reported the use of split bands of abdominal wall consisting of fascia, peritoneum and muscle, which were attached to the abdominal wall at one end, the other being used as suture material.

Kocher[7], in 1902, applied crushing stomach clamps to the cut liver edge. The clamps were brought out through the abdominal wound and removed in forty-eight hours.

In 1905, Cullen[8,9] used an overlapping-mattress-suture technic with a modified Kousnetzoff needle for controlling hepatic hemorrhage.

Gillette[10] passed five or six sutures of catgut through the entire liver substance, brought them through the chest wall around a rib and tied the sutures on the skin. In 1905 he reported 2 such cases with recovery.

Boljarski[11], in 1910, used isolated omentum and catgut sutures for control of liver bleeding.

Controlling hemorrhage by utilizing the hemostatic elements in the blood itself was first introduced by Cushing[12] who used striated muscle in neurosurgery as a hemostatic plug and later applied it to liver biopsies, reporting the results in 1911. Striated muscle controlled hemorrhages because thrombokinase, liberated by the damaged muscle, aided in blood clotting and also the muscle plug by its bulk caused hemostatic compression of the liver sinuses.

In 1915 Grey[13] used sheep's fibrin in small blocks for hemostasis, and Harvey, in 1918[14], used beef fibrin in small sheets for similar purposes.

Seegers and his coworkers[15,16] discovered thrombin in 1938 and used it as a hemostatic agent in human beings and animals in the following year.

Ingraham et al[17-21], in 1944, used human fibrinogen foam and fibrin foam for hemostasis in neurosurgery and showed the value of these substances in general surgery. They found these products absorbable, nonirritating and more effective in combination with thrombin.

In 1943 Frantz employed oxidized cellulose (oxycel) to arrest hemorrhage from brain, liver, kidney and spleen in animals. The oxidized cellulose was prepared from gauze or cotton and subjected to an oxidation process, which produced cellulosic acid. Hemostasis was a result of the action of this acid, and no advantage was obtained by the use of thrombin with oxycel because thrombin became inactive in an acid medium. The oxycel turned black on contact with blood and was completely absorbed in three or four weeks. It was probably absorbed by phagocytosis and by dissolution as small particles into the blood stream, which were excreted subsequently by the kidneys. Tissue reaction to the oxycel was minimal[22-25].

Light and Prentice, in 1945[26,27], used a gelatin sponge (gelfoam) for hemostasis in surgery. The gelatin sponge was made from ordinary commercial gelatin

by the introduction of air into a gelatin solution to obtain a porosity. This sponge was then heated in an oven until dry. The hemostatic action of the gelatin sponge was twofold: it acted as a tampon and also liberated thromboplastin from damaged platelets that entered its foamy structure and became traumatized by contact with the walls of its interstices. Gelfoam was hemostatic when used with or without thrombin and was absorbed in fifteen to twenty-four days with minimal tissue reaction.

Levitski[28] chose a hemostol plug for hemostasis. The hemostol plug was made from relatively fresh coagulated human plasma. He used 100 parts of citrated plasma from blood three to five days old and added 5 parts of calcium chloride to coagulate the plasma. The coagulated plasma was transferred to a sponge, and the serum squeezed out of it. The hemostol plug was inserted into the liver wound for three to five minutes, after which hemostasis and adherence took place. This

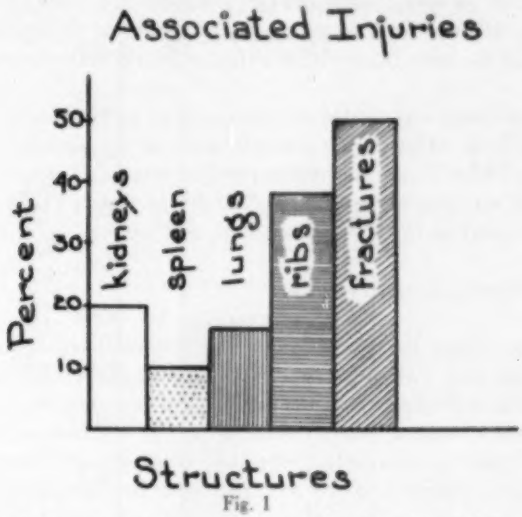

Fig. 1

plug of coagulated human plasma was completely absorbed, and the tissue reaction to it negligible. This process is cumbersome.

In 1946, Lowry[29] used synthetic adhesive tape in treating wounds of the liver. After resecting sections of rabbit livers, he applied two strips of Scotch tape, in the form of an envelope, to the liver. The entrapped clot acted as a plug and controlled the hemorrhage. Small localized encapsulated abscesses or caseous residues surrounded by fibrous tissue were usually found at the end of a month of such treatment.

Jenkins, in 1947[30,31], applied gelfoam by a blanket technic to control wounds from the liver in animals; he also applied it to the aorta by a cuff technic and to the vena cava and the heart by a patch technic.

The authors[32] recently reported three cases of trauma to the liver in humans successfully treated with oxycel and gelfoam.

Cause of Ruptured Liver

This paper will limit itself to the experience with this condition at the Boston City Hospital between the years 1935-1945 inclusive; a total of forty cases. Only the cases with subcutaneous or nonpenetrating liver injuries are considered.

Approximately ten cases of ruptured liver are admitted to the surgical services of the Boston City Hospital each year; not all of these have sufficient clinical data for proper evaluation. Though this figure may seem low it is comparatively high inasmuch as many larger hospitals admit only one or two cases yearly.

Hepatic trauma resulted from crushing injuries to the abdomen in two cases; one from being crushed in an elevator shaft, and the other by being pinned up against the wall by a truck. Falling from a height accounted for six cases, most of which were due to attempted suicide. Falls from slight elevations, such as down a few stairs, was responsible for two cases, while coasting accidents and direct assault accounted for three more. About two-thirds (26 cases) of all the ruptured livers were due to some form of automobile violence. It is interesting to note that while rupture of the liver occurs quite often, rupture of the spleen is by far more frequent.

There were thirty-two males as compared to eight females in this series—a rate of four to one. Most of the patients were in the second, third, and fourth decades of life. Three cases occurred in the 1-10 year age group, nine cases in the 10-20 age group, six cases in the 20-30 and 30-40 age group. Three cases in the 40-50 age group, five cases in the 50-60 age group, and one case in the 60-70 and 70-80 age groups.

Figure 1 shows associated injuries.

Mortality

The total mortality for subcutaneous injury to the liver, regardless of the type of treatment was 62.5 per cent (25 cases). The mortality for nonoperated cases was 81.8 per cent (18 cases). On the other hand the mortality in those operated was 38.9 per cent (7 cases). When chemotherapy in the form of sulfonamides and operation were used, the mortality dropped to 33⅓ per cent (6 cases). Glancing at these figures it is evident that the mortality rate in rupture of the liver is very high (Fig. 2).

Boljarski's[33] mortality rate (1914) for subcutaneous liver injuries was 88 per cent while Thole[34] found the operative mortality in both subcutaneous and percutaneous rupture of the liver to be 39 per cent. Madding[35] reported a mortality rate of 27 per cent in 829 cases of all types of liver injury in World War II, regardless of the type of treatment. Our figures coincide with those of Thole[34], while Boljarski's figures seem high and those of Madding not representative for the purpose of this report.

Amount of Liver Necessary to Sustain Life

Of interest to this group is the amount of trauma and blood loss the liver can endure and still retain its function.

Mann[36] (1927) removed as much as 50 per cent of liver tissue in animals without any serious impairment of liver function. He also demonstrated that liver

tissue has remarkable powers of regeneration and recuperation. Ireneus and Puestow[37] in 1944 removed as much as 90 per cent of liver tissue in dogs in successive intervals with survival. They also showed that the functional reserve of liver is unimpaired after massive blood loss from partially hepatectomized animals. In 1947 Martin[38] disclosed that in dogs the usual functional liver tests, such as

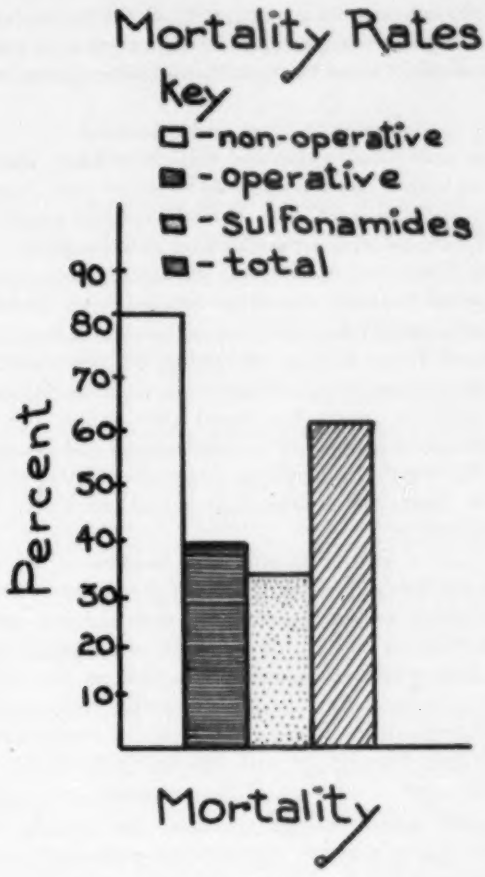

Fig. 2

bromsulfalein excretion, galactose tolerance, prothrombin time and alkaline phosphatase are not affected to any appreciable extent after massive trauma to the liver when as much as 50 per cent of the liver was damaged.

This parallels our experience in humans for in our recent cases all the accepted liver function and excretion tests were carried out routinely and were well within normal limits.

The operative mortality has been markedly reduced; by our knowledge and use of transfusion technics to combat hemorrhage and shock; by benefiting from past experience; (namely the optimum time of operation); by the use of antibiotics and more recently by the use of absorbable hemostatics.

The last two factors, the antibiotics and hemostatic agents, must play a distinct role in lowering our mortality rate because since the advent of transfusion and our knowledge of the use of parenteral fluids all the patients had been adequately treated for shock and appeared to be clinically out of shock, at the time of operation. In spite of this without hemostatics we had an operative mortality of 38.9 per cent.

Optimum Time for Operation

Surgery, when performed within the first three hours after hospital admission, was associated with a mortality rate of 33⅓ per cent. After three hours the mortality rate rose to 66 per cent, after twelve hours the operation mortality rate dropped to zero. This may seem a paradox and would suggest a waiting period in all cases of twelve hours, but these cases indicated minor injury with minimal hemorrhage, where the diagnosis was either delayed or so obscure that rupture of the liver was an incidental finding and had taken care of itself. Thole[34] found an operative mortality of 39 per cent in penetrating and subcutaneous injuries of the liver the first six hours after injury; 50 per cent, six to twelve hours after injury; and 67 per cent, twelve to twenty-four hours after injury. This last figure seems high but at the time of his report (1912) whole blood and plasma were not available. Our figures indicate the value of early operation within the first three hours after trauma to the liver, and a critical period of operability between three to twelve hours after injury.

Use of Hemostatic Agents

Regardless of the type of treatment used in this series of forty cases previous to the use of hemostatic agents the mortality was 62.5 per cent. The operative mortality for subcutaneous rupture of the liver using gauze, muscle or cat-gut sutures to control hemorrhage mechanically was 38.9 per cent. To lower this mortality and postoperative morbidity the authors sought new operation criteria and technics. It has been shown in animals with ruptured livers that recovery can be enhanced by controlling hemorrhage with absorbable hemostatic packs.

The work of Frantz[22] in 1943 with oxidized cellulose (oxycel) and Light and Prentice in 1945, with gelatin sponge (gelfoam) has already been described in detail, earlier in this paper, together with their properties of hemostasis.

We have found that in cases of ruptured liver in the human, whenever the abdomen was not drained, postoperative complications such as subphrenic abscess, biliary fistula, abdominal wall abscess and ventral hernia did not occur. Simple packing of the laceration with absorbable hemostatic sponges, suture of absorbable gelfoam or oxycel sponges to the liver capsule or packing of the liver laceration with oxycel or gelfoam combined with suturing of the liver capsule to the diaphragm to prevent the suction effect of the diaphragm from displacing the pack, invariably controlled the hemorrhage. This technic, plus closing the abdomen tight

without drainage, reduced our operative mortality in the last four cases at the Boston City Hospital to zero.

Summary

The literature on control of liver hemorrhage following trauma has been reviewed and a series of forty cases treated at the Boston City Hospital previous to the use of absorbable hemostatic agents analyzed. Although four cases is a small number from which to draw conclusions, nevertheless the operative mortality falling from 38.9 per cent to zero is significant and points to the value of absorbable agents which completely stop the hemorrhages allowing the abdomen to be closed without drainage.

Liver function is not materially impaired either directly from the trauma or in the process of repair and regeneration following the trauma.

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Discussion

Dr. Lester R. Whitaker (Portsmouth, N. H.):—Dr. Papen has had a wonderful opportunity to work in this field, such as many of us have not had. We are likely to think that wounds of the liver are rare and not very important, but Dr. Papen has mentioned that the critical period is three to twelve hours. That means that whoever sees the case, especially if he does any surgery at all, has got to handle it. So it behooves all of us to know all we can about the subject.

My experience, probably like that of most others here, has been very limited. It has been chiefly with work on animals, and also on that trauma of the liver brought about too often by an overenthusiastic assistant in a gallbladder operation, or even by an impatient surgeon himself, when the liver is ripped. That has to be handled, too, and is the most common cause of trauma to the liver.

If we use animals, we can reproduce a situation and experiment with handling it. Now, in case any antivivisectionists have sneaked in here, I wish to say that in any experiment which I have done, the liver-trauma was produced after the animal was under an anesthetic. The liver was cut and then methods of stopping the bleeding tried. That was before we had these hemostatic agents which have performed so wonderfully in Dr. Papen's hands.

At that time a great deal was being said about the electrosurgical unit. It seemed all you had to do was to point the electrode at a bleeding liver and the bleeding would be magically stopped. But there is one thing to remember. Figuratively speaking it is that you can't push up Niagara with a hot poker. Neither can you stop active bleeding in the liver, or any other parenchymatous organ with a little "squizzling" with an active electrode of an electrosurgical unit. You are wasting your time and losing blood while you are trying that.

The pressure pack is the immediate method that every surgeon uses for stopping hemorrhage. If he gets a sudden hemorrhage, he throws in a pack at once, and then he has time to plan how he is going to get it permanently stopped. There is a use for the electrosurgical unit, particularly in superficial wounds of the liver, if they are not bleeding too freely, by using a flat electrode and pressure, with a

heavy coagulating current, particularly around the edges of the wound. You pack the wound itself and then, by applying the ball or blade electrode with heavy electrocoagulation, you can coagulate that liver to a depth about the same as you see it spread laterally. That does stop the bleeding where the liver is coagulated, but that doesn't take care of the bleeding in the depths of a wound. The only way that you can handle that with an electrosurgical unit is in some way to get the bleeding under temporary control, and then electrocoagulate the tissue in the depths of the wound. That is very difficult, and I believe the pack method of Dr. Papen is better.

The reason why you can't stop the actively bleeding hemorrhage by electrocoagulation is that the blood coming out dissipates the heat of the diathermic current going through. Dr. Papen has pointed out that with the pack method results are better without drainage. This holds for electrosurgery. The electrocoagulum will usually be absorbed. If a cyst results, it can be drained afterwards. However, I believe with Dr. Papen that for deep liver wounds the best method of control is the fixation of an absorbable pack.

Dr. George W. Papen (Boston, Mass.):—I was under the impression that probably this subject would not arouse much discussion for it is unusual, and there is very little in the literature about it especially, as to the use of these agents in the human. However, I feel that you who do surgery, or use surgeons as consultants, should go away from here having them in mind. You never know when you will get into a case of ruptured liver and find a belly-full of blood from a stellate crack in the dome of the liver, and you just can't wait until you can get some thrombin or fibrin foam, if there isn't any at hand. We all have in our operating rooms these hemostatic packs to stop nosebleeds, and for use in prostatic surgery. Don't hesitate to use them in this emergency. They are absorbed and set up very little foreign body reaction. They all cause a fibroplasia within three or four days, and will be absorbed within eighteen to twenty-six days after their use.

About the electrosurgical unit; there again, Dr. Whitaker, it can be used in superficial bleeding of the liver, but if you find the deep areas of the liver damaged, there is so much bleeding and so much bile pouring out, the heat loss is so great that you get a coagulum which is merely mush, and you can't do much about it without superimposing a third or fourth degree burn on an already severely injured liver.

I have been asked a question off the record, which I prefer, oxycel or gelfoam. I prefer oxycel because it is more workable; gelfoam, when it becomes moist, becomes slimy and it slips around, and it is hard to fix in position; however, if you don't have oxycel the following technic can be used when you have only gelfoam: Pack the sulcus of the liver with gelfoam and hold your finger there for about two or three minutes, and in spite of previous active bleeding, you will be surprised that when you take your hand away, the field will be dry, and then, to prevent that pack from being pushed out by the suction action of the diaphragm, take a few sutures through Glisson's capsule of the liver to hold the pack in place.

I have given up, and I know Dr. Arthur Allen, of Massachusetts General Hospital (I heard a paper he read about ten years ago), has given up packs in the liver. When we open the abdomen and find, a belly-full of blood, to be sure, there is some panic. You have a sick patient on the table, and the first impulse is to pack the rent in the liver. Don't do it! Even if you don't have gelfoam, or you don't have oxycel present, use the hemostatic agent the blood of the patient has, namely, your blood clot. Never remove a blood clot from a ruptured liver unless you have something else to put in its place, like thrombin, oxycel, or gelfoam, because we all know that if you pack a liver and then you go to remove that pack—and I used to be always scared to death about removing it—you have to give an anesthetic; even if you tease it out gently, what do you get? Secondary hemorrhage or secondary infection.

Dr. Whitaker:—I have an idea when you say "do not pack the liver", you mean not pack it and leave it.

Dr. Papen:—You could pack it temporarily if there was considerable acute bleeding, until you could find yourself, and decide what you wanted to do until the hemostatic agent was ready.

Dr. Whitaker:—That is exactly right. I am sorry if I misunderstood.

Dr. Papen:—Yes, I am sorry if I misinformed you. I meant, not to leave the pack in the liver for several days, which has been done in the past. All one has to do is to place a sponge with pressure on the liver sulcus and suck out the blood from the abdomen while you are holding the pack in place, get your oxycel or gelfoam ready and replace the pack with them; then place a couple of through and through sutures in the capsule; but don't leave a gauze pack in the liver. They don't do well.

GASTROENTEROLOGICAL CONDITIONS AND COMPLICATIONS IN THE COURSE OF DIABETES MELLITUS*

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Cancer in the diabetic presents an unrivalled opportunity for early diagnosis and cure. Statistics do not allow an inference that it is more or less frequent in diabetes, although cancer as a cause of death in diabetes has risen from 1.5 per cent between 1898-1914 in our series to 8.9 per cent in 1944-1949. This is accounted for by the patients living 14.4 years instead of 4.9 years and dying at 64 instead of at 44 years of age.

In the last eleven years, September 1937 to September 1948, there were autopsies upon 128 of our cases revealing cancer, and among these were 37 of our patients with cancer of the digestive tract. The distribution was as follows: Mouth and pharynx 4, stomach 7, colon 16, rectum 10. As yet we cannot prove our results in the diagnosis and treatment of cancer of the digestive tract are better than for nondiabetics, but we are closely watching our series and earnestly striving to diagnose them earlier and earlier. (We know that one case of cancer of the stomach in a potential diabetic lived 7 years and 4 months.) Several of the patients with malignancy of the bowel have lived many years

Right here I would ask for opinions about the desirability of proctoscopic examinations upon our diabetic clientêle. At what age should they be made routine and how frequently should they be repeated? Remember our patients belong to a low income group and the chief endeavor is to have them return to their own physician or to us for examination every three months, and that more than a quarter of those who have died have lived over twenty years. If a proctoscopic examination is necessary for a new patient, how frequently should it be repeated in an old patient?

The old diagnostic teaching rule that all symptoms should be explained by a single diagnosis falls flat in diabetes. We know that irrespective of what the real presenting trouble is that we are dealing with a group, who overwhelmingly are riddled with arteriosclerosis and that this holds after fifteen years, even for those who contract the disease in childhood.

Operations were performed for cancer upon 35 cases of the digestive tract between 1940 and 1949, esophagus and fundus of the stomach 1 case successfully resected, stomach 6, cecum 3, transverse colon 3, descending colon 2, sigmoid 8, and rectosigmoid and rectum 12.

The range of age in the 35 cases was from 44 to 76 years of age, the highest incidence being in the 60's. Anemia was prominent and in many instances the

*Presented before the Postgraduate Course in Gastrointestinal Surgery of the National Gastroenterological Association, Boston, Mass., 27, 28, 29 October 1949.

carcinoma was discovered during the course of investigation for anemia. The average hemoglobin for the group was 12.4 mg. Twenty-four patients had major surgery in the form of resections. One patient had four separate carcinomas of the colon at different times and has survived four resections. It is of considerable interest that in spite of the poor risk type of patient and the magnitude of the procedure there was only one serious complication in any way related to diabetes in the 35 cases and that was a cerebrovascular accident following a transverse colostomy. Although many patients died later of recurrence or coronary thrombosis, there was only one hospital death. This followed a successful, large bowel resection. The autopsy failed to reveal the cause of death.

One of the patients with cancer of the descending colon, which was successfully removed, a few days after the operation developed acute gallbladder symptoms and was reoperated upon for gallstones with success.

May I register a warning in the management of gastrointestinal disease? It is, namely, this, that the treatment, dietetic and medicinal, is often so good that it obscures and conceals the diagnosis with disastrous results. Gain in weight and cessation of alternating diarrhea and constipation are all too frequently obtained by simple adjustments of diet and medicines. *Vorsicht! Prenez-garde!* Don't treat medically a patient with indigestion too well! He may harbor malignant disease and you may be hiding it.

Ulcerative colitis—Nocturnal diarrhea:—Ulcerative colitis is rare in a diabetic clientêle. This seems surprising, because diabetics eat a large quantity of coarse foods. Even in the days of bran breads, washed bran, now in oblivion, we seldom saw cases and one does not miss such a diagnosis. The use of bran led to so many occurrences of an impacted rectum requiring the digital attention of the doctor that we all cheerfully renounced it. Nocturnal diarrhea, however, is not infrequent. Sheridan and Bailey[1] of our group reported 40 cases in 1946. More and more, this has come to be explained on the basis of diabetic neuropathy and the fact that many of these cases improve after months of discomfort confirms it. Undoubtedly the absence of hydrochloric acid and the coarse and large diets are contributory factors, because one seldom, if ever, meets this distressing complication in the diabetically controlled patient. In the above series the injection of crude liver extract was effective in a large percentage of the series. In this connection I would call attention to a recent paper by Rabinowitch[2], in which the frequency of achlorhydria in diabetes is associated with anemia and neuritis and a reason therefor presented.

The preparation of a diabetic for surgery is simple. The operation should take place in the early morning without food or drink having been taken since the previous evening. If quick-acting insulin and protamine zinc insulin have been employed, the former is omitted, the dose of the latter before operation is usually halved and the remainder given at the conclusion of the operation. Regular or crystalline insulin may also be injected subcutaneously at this time, because the patient will probably receive glucose in saline to offset his lack of breakfast. We

never give insulin in the glucose or saline liquid, because its action would be too uncertain. For the balance of the day we use the Benedict insulin unit fraction prescription $\frac{\text{Red — Orange — Yellow — Green}}{16 \quad 12 \quad 8 \quad 4}$ every four hours, remembering that the first specimen of urine voided after an operation or glucose is valueless, because it usually is red and represents a temporary state, and insulin given to offset it may result in a reaction.

Unobtrusive gastrointestinal emergencies are constantly arising in our cases with diabetic coma. The first I will mention is a dilated stomach—gastric atony. Seeing one such case will keep this complication vivid for a lifetime, for undiagnosed it can lead to death, just as I understand overdistention of the stomach of an animal will arrest the heart. This is the reason for our standard rule in the treatment of coma to be sure to empty the stomach and to do it very, very gently, because the process is a precarious one and carries a hazard. We use a large stomach tube, because the stomach may be retaining coarse food consumed two days earlier. Apparently this condition of gastric atony will result when acidosis—ketonuria—develops, irrespective of whether in diabetic coma or as in childhood following vomiting, as a result of anesthesia, particularly with the use of ether. Both experimental and clinical evidence support this idea, although often years ago I saw it occur when acidotic patients avidly drank ice water in large quantities. Incidentally, in coma, liquids are prescribed by us only in 50-100 cc. quantities every hour and in teaspoonful doses until the stomach is functioning normally.

A second gastrointestinal complication of diabetic coma is gastric hemorrhage. Usually this is of old, dark blood, long resident in the stomach. It is most common to find it and so common that it may divert the unwary from the recognition of a peptic ulcer, which was the reason for it in Case 17478. Unless this blood is removed by lavage, vomiting persists and feeding is useless.

The third complication is a pseudoperitonitis or a true appendicitis. This was recognized as long ago as Kussmaul's original description of coma. The symptoms conform closely to peritonitis, the Hippocratic facies, the tense abdomen and even the leucocytosis. That they are not necessarily due to appendicitis was shown in Berning's case[3], because the appendix had been removed several years before and they recurred in the several, subsequent coma bouts of his patient. The symptoms and signs resemble the condition, more rarely met in the chest, when dehydration in coma is so extreme that a friction rub can be heard. I am in hopes that the depletion of the excretion of sodium chloride in diabetic coma can be demonstrated in part to be due to abnormal functioning of the suprarenal, because that might give a new lead in treatment. At least it confirms us in our liberal use of saline.

It may be an exaggeration to say that we ask a surgeon to see in consultation every case of diabetic coma we treat, but it is not far from the truth, especially when dealing with coma in children. The abdominal distress and distention and

the leucocytosis, all common to coma and appendicitis, make the differential diagnosis difficult. The existence of diabetic coma is no excuse for a death from appendicitis, particularly when two hours' observation by surgeon and physician will solve the situation. Both conditions can and do simultaneously exist. This opens up for discussion the subject of appendicitis in diabetes. I remember well my first case in the very early years of this century, when in cold blood a grumbling appendix was removed. Today we err on the side of advising an operation in all doubtful cases, and especially in that group of patients with repeated attacks of right lower quadrant pain so as to eliminate completely one source of confusion and danger.

Appendicitis in diabetes is the same as in the nondiabetic, but it is veritably almost symptomless. At least five times in the last ten years acute appendicitis has developed on the wards in patients hospitalized for some other condition. Two developed it within three days of another operative procedure. Repeatedly one encounters it in children with scant manifestation, so that the chief worry of the doctor in a summer camp for diabetic children is that it may be overlooked when the patient is fifty miles from the hospital. I still remember that patient in the corner bed of Ward 221 who, with the accompaniments of syphilis and gangrene in an extremity, developed his appendicitis uncomplainingly and went on to a fatal issue.

Between October 1940 and October 1949 there occurred 24 cases of acute appendicitis, of which 15 were unruptured and 8 ruptured with abscess formation, and one with a generalized peritonitis. Interval operations for appendicitis were done in 17 cases. No age was spared in the acute group, the ages spreading from 8 to 74 years. In general there was a long delay between onset of symptoms and operation, for the unruptured cases 22 hours and the ruptured cases even 4½ days. The shortest interval between onset of symptoms and operation was 10 hours. During this 9 years and 9 months period studied, with a total of 41 cases operated upon, there were probably about 12,000 hospital admissions for diabetes on our service.

Some degree of pain and tenderness was present in all cases of appendicitis, and nausea or vomiting in three-fourths. In the acute cases the temperature varied between 98 and 100.2, the average being 99.5. This finding is similar to the low temperature encountered with diabetics having tuberculosis. The average white count was 16,000 in the acute cases and 20,000 in the ruptured. There were three deaths—one a patient who entered in extremis after an illness of two weeks, not operated upon; another a patient whose appendix was ruptured on admission with general peritonitis followed by rib resection for hepatic and pulmonary abscesses; and a third a patient who died of coronary thrombosis and pulmonary emboli following incision and drainage of an appendicial abscess.

Although some patients complained of discomfort rather than pain, there usually was a history of discomfort beginning in the epigastrium which later shifted to the right lower quadrant, thus aiding in making the diagnosis. One

patient, for instance, worked for two days after onset of symptoms and drove himself to the hospital with a full-blown appendicial abscess. The tenderness, although often minimal, was usually well localized. It was the rule rather than the exception to find the local pathology all out of proportion to the symptoms and signs, that is, a gangrenous appendix with minimal discomfort and tenderness.

Could the mildness of symptoms in diabetics with appendicitis and in peptic ulcer be in part due to a coexisting neuropathy in some cases?

Among the 10,673 of our fatal cases of diabetes there were 56 reported to have died of appendicitis, or 0.47 per cent, or 1 death in 254.

Peptic ulcer was almost unknown in our diabetics in the early years of the century. This was easily explainable by their short duration of life. Whether it is more or less frequent in diabetics than nondiabetics, I do not know. The diabetic diet does not predispose to ulcer. Again, among our 10,673 fatal cases there were but 27 instances in which death was attributed to this cause. However, in 332 autopsies upon diabetics of our group between September 1937 and September 1948, Dr. Shields Warren and Dr. Philip M. Lecompte encountered 7 ulcers, in two of which the bleeding ulcer led to a fatal issue. Unobtrusiveness of symptoms was characteristic of the group, just as with appendicitis. For example, one man with a large gastric ulcer was symptomless and the ulcer only found in a search for a severe anemia. Another admitted only gastric soreness and yet had a large gastric ulcer which had penetrated into the pancreas.

In the Mayo Clinic, among 2,584 diabetics, ulcer was diagnosed in 61, or 2.3 per cent.

Among 12,000 cases observed at the George F. Baker Clinic of the New England Deaconess Hospital between 1934 and 1944, there were 94 cases of peptic ulcer, or 0.89 per cent, males 68, females 26. These cases were reported by Wood[4] and the following data in chief part are from his paper. Seventy-three of the patients were above the age of 40 years. Seventy-four had a single duodenal ulcer and ten a single gastric ulcer. In fifty patients typical ulcer pain was lacking. Severity of the diabetes was unrelated to the ulcer. Seven of the ulcer cases subsequently had diabetic coma. The ulcer apparently had been long neglected, or overlooked, because after it had existed an average of 6 years, 54 of the 94 patients had massive hemorrhage, obstruction, perforation or gastric carcinoma. Arteriosclerosis was prominent in 42 patients, thus posing a special factor because of hemorrhage. A perforation occurred in 10 cases, and 32 cases had obstruction as demonstrated by x-ray. Major operations were performed in 13 cases of the 94. There were two postoperative deaths. In a subsequent follow-up, replies or visits showed 40 were completely relieved, 20 improved, but in 34 there was a recurrence of serious symptoms, a rather gloomy picture. In the following period of five years ending in October 1949, there occurred six more cases of peptic ulcer which were operated upon.

The surgery of the diabetic must be of the highest quality, because the diabetic is certainly not as good a risk as a nondiabetic. I often wonder that the

surgeons dare to operate on our cases. Each year adds to the number of diabetics of long duration and of older ages, and until we have better methods of treatment these cases will present more and more arteriosclerosis.

In the last fifty years the duration of life of diabetics has trebled and in the next fifty years it can double even without new discoveries. To attain this end it is essential that at each visit of a patient to a doctor, the diabetic treatment and control of the disease must be revised and improved and a careful search made for complications diabetic and nondiabetic.

How seldom it is one sees a diabetic patient with whom one can feel satisfied with the previous course of care prescribed or followed.

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COMPLICATIONS AND SEQUELAE OF GALLBLADDER DISEASE*†

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This presentation concerns the conditions associated with, and secondary to gallbladder disease such as cholangitis, pancreatitis, gastritis, nutritional disturbances and cardiac conditions. These conditions arise largely as a result of reflex disturbances from impulses originating in the diseased gallbladder and conducted through the vagus nerve. The secondary condition may persist long after the offending gallbladder has been removed. The surgeon and gastroenterologist, therefore, should be qualified to recognize and treat the secondary condition either concurrently with the elimination of the original focus in the gallbladder or after the gallbladder has been removed. It is necessary for the physician treating patients with gallbladder ailments to have a thorough understanding of the anatomy and physiology involved. The gallbladder and biliary tract is at the crossroads of nutrition. It has been said that the way to a man's heart is through his stomach. The way to all persons' organs is through the adequate digestion of the nutrient elements taken into the alimentary canal.

Cholangitis

Mechanism:—In 1935 we reported a method for measuring pressure in the common bile duct[1]. As a result of studies carried out according to this method and repeated over the years[2,3,4] it has been found that cholangitis is associated with a spasm of a second portion of the duodenum. Many authorities in the past have referred to the spasm of the sphincter of Oddi and the resulting back pressure in the common bile duct producing biliary stasis. Terms such as postcholecystectomy syndrome and biliary dyskinesia have been introduced to designate conditions in which the patient continued to suffer symptoms after the gallbladder had been removed. It is my belief that these conditions are due to cholangitis, that is, an inflammatory condition within the smaller radicles of the biliary tree. The resulting back pressure in the biliary tree produces pain setting up a reflex producing spasm at the duodenum with further back pressure, stasis and infection. In the postoperative study of patients with indwelling T-tubes, according to methods previously described, it was found that following the operation at first the perfusion pain level, an index of cholangitis, was as low as 100 mm. of water. Gradually with continued T-tube drainage this pain level improved up to 500 mm. of water, indicating that the cholangitis had cleared up and that the T-tube could be removed. Frequently, at the same time, the resting intrabiliary pressure, an index of the ease with which bile can flow into the duodenum, became reduced to 30 mm. of water or better. One can readily imagine that a patient who has inflammation within the biliary tract to the degree that pressure as low as 100 mm. of water would produce pain could certainly be expected to suffer attacks following removal of the T-tube.

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*Presented before the Postgraduate Course in Gastrointestinal Surgery of the National Gastroenterological Association, Boston, Mass., 27, 28, 29 October 1949.

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Also, one can readily understand that there must be many people who suffer pain from cholangitis without ever having had the benefit of T-tube drainage.

Symptoms:—The symptoms of cholangitis are those usually attributed to gall-bladder disease. The patient complains of fullness, gaseous distention, the clothing is too tight, they have a sensation of gas, frequently in the substernal region. The patient states that there is gas that will not go up or down. The distention of a hollow viscus is frequently referred to by the patient as gas. At times the pain is severe. It may be located in the midepigastrium, in the substernal region, in the right upper quadrant, or it may be radiated to the right or left scapular region. I have on many occasions reproduced this exact pain by perfusing saline solution into the common bile duct of patients with T-tubes. However, in such patients, the sensitivity to pressure decreases with continued T-tube drainage, indicating the original cause being due to infection. It has been found in the past and has been repeatedly proven that morphine sulphate and related drugs produce spasm of the duodenal wall. Frequently, these drugs will precipitate an attack of pain in persons suffering from cholangitis and the nitrite drugs which relax the duodenum and allow a free flow of bile will frequently relieve the pain.

Diagnosis:—The diagnosis of cholangitis is confirmed by finding a low pain level when the common duct is perfused. An acute cholangitis usually is associated with pus draining freely from the T-tube. In the patients in whom the tube has been removed or those that have not been operated upon, the symptoms of cholangitis can be confirmed by finding pus in the duodenal drainage.

Treatment:—The best treatment for cholangitis is prolonged drainage of the common bile duct with a T-tube. We have previously described a T-tube suitable for this type of drainage[4]. If the T-tube is in place, the injection of streptomycin into the T-tube will facilitate recovery from this condition. This T-tube must be left in for a long time until the following conditions are met: 1. The perfusion pain level must be better than 500 mm. of water pressure. 2. The resting intrabiliary pressure, an index of patency of the ampulla of Vater must be no more than 30 mm. of water level above the ensiform. 3. Cholangiograms must show a patency of the lower end of the bile duct, the absence of pancreatitis and stones. We have practiced this method over the past ten years with excellent results. In the case of the patient who had previously been operated upon in whom the T-tube had been prematurely removed or who had not the benefit of T-tube drainage and subsequently developed pain similar to that before the operation presents a different problem. In this patient one may bring about relief by the administration of nitroglycerine, 1/250th under the tongue in doses of one to two tablets every three hours for several days and three times a day after meals and at bedtime thereafter. If this treatment is carried out for a period of three weeks it will result in a cure in many cases. However, there are a certain percentage that will not respond to this treatment in which instance it is necessary to do repeated duodenal drainages in the following manner: After the Levine tube has been passed into the duodenum, 60 c.c. of a saturated solution of magnesium sulphate is injected. This is left in for 30 minutes and then the duodenum is irrigated with warm water. This irrigation is

repeated during which time the patient is given inhalation of amyl nitrite approximately every twenty minutes to relax the duodenum. This will usually produce a free flow of bile. The administration of bile salts to this type of patient is also probably beneficial since the choleretic action of bile salts would tend to wash out the bacteria from the small radicles of the biliary tree. However, before bile salts are administered, one should be reasonably certain that all causes of obstruction such as spasm has been removed by proper medication. In a few cases it will be necessary to reoperate and put in a T-tube. In exploration of the bile duct in such cases, one should dilate the ampulla of Vater up to a 6 mm. Bake's dilator. Excessive dilatation of the ampulla will only result in edema, further fibrosis and a further narrowing. I have not found it necessary to put in a long-limbed T-tube going through the ampulla of Vater. Instead I have found it suitable and adequate to drain the common bile duct with a short-limbed T-tube, in this way permitting the normal function of the ampulla of Vater and the sphincter of Oddi. I firmly believe that bile which is free of infection has a very low surface tension and will run freely through a fairly small hole. On the other hand, if there is any infection present, then mucus plugs will rapidly produce an obstruction. Prolonged T-tube drainage with repeated instillations of streptomycin results in complete clearing-up of the infection. The bile acids then will keep the bile at a low surface tension. On the other hand, if infection, particularly with the B-coli is present, the bile acids are split and the crystalloids in the bile are precipitated resulting in mud and finally stones.

Recurrent Pancreatic Edema

Recurrent pancreatic edema is much more frequently associated with gallbladder disease than is commonly believed. I am sure that if the pancreas is carefully examined in its entirety, not only the head but the body and the tail, this condition will be found much more often.

Mechanism:—There seem to be two definite types of conditions producing this complication. These may be described as 1) the regurgitation theory, and 2) the neurogenic theory. The regurgitation theory presumes that initially there is narrowing of the ampulla of Vater, possibly due to a stricture or stone, producing a reflux of bile into the pancreatic duct resulting in activation of the trypsinogen to trypsin which forms the irritant resulting in the pancreatic edema. It is my opinion that this theory will explain a great number of cases. I have often found that in this condition when the cholangiograms are taken, the pancreatic duct is visualized. It is my belief that in these cases there is also a reverse flow of pancreatic juice into the biliary tract since these people are very prone to cholangitis. Also the condition seems more common in men in which case the biliary lesion is usually an obstruction at the cystic duct, at first intermittent and later permanent, with or without the development of stones.

The second theory, the neurogenic theory, results from research work performed by Dr. Stephen J. Maddock[5] at the Boston City Hospital. In this work he showed that if the pancreatic duct of the cat is ligated, nothing unusual happens so long as the cat is kept on a diet which is not irritating to the stomach and she

lives in an environment conducive to peace of mind. However, if, on the other hand, she is fed food that is irritating to the stomach lining, or if she is agitated by the presence of unfriendly dogs, the pancreas will actually be destroyed by the action of its own juices. These experiments suggest that the impulses originating in the stomach or in the cerebrum pour down through the vagus nerve, liberating the trypsinogen which, finding no outlet, becomes activated by tissue juices, producing an irritation and destruction of the pancreas. By applying these findings to the human, we can explain many situations associated with pancreatic edema which are not explained by the regurgitation theory, such as, the frequency of acute pancreatitis, following gastritis from alcoholic indiscretions. I have also noted the flare-up of pancreatitis following periods in which the victim was under a great mental strain. In the case of the human, therefore, there are three foci of these injurious impulses, the most common being a diseased gallbladder, in which impulses are set up travelling to the central nervous system where they are multiplied a thousand times and relayed down through the vagus nerve, setting up a release of pancreatic juice and resulting in edema. Also, the stomach may be a focus of impulses as following alcoholic or dietary indiscretion. I have also seen reflex pancreatic edema, sufficient to obstruct the duodenum, produced by a high gastric ulcer. The third source of impulses are from the cerebrum. A person under great stress and strain of worry frequently will be stricken with an attack of pancreatic edema. The term pancreatic edema is used in contradistinction to the more severe and advanced state frequently known as acute pancreatitis.

Symptoms:—In acute pancreatic edema, the pain is located in the epigastrium. It frequently radiates across to the left. A saddle pain is described in the upper lumbar or lower dorsal region extending across the back. The patient frequently obtains relief when he sits up and leans forward.

Diagnosis:—On physical examination, there is tenderness in the midepigastrium usually on deep palpation. The urinary diastase may be elevated temporarily during a severe attack but usually is not during the time that the condition is chronic.

Treatment:—The treatment consists of operation, removal of the offending gallbladder, drainage of the common bile duct until all cholangitis has disappeared and until there is no further pressure from the head of the pancreas as indicated by the biliary dynamics previously referred to. The treatment of a case which is not operated upon or one that occurs after surgery, is essentially medical. Sedatives to allay the cerebral impulses, belladonna or related synthetic drugs to cut down the impulses pouring down through the vagus nerve, a very bland diet to reduce the digestive impulses to the minimum will usually produce relief in a week or two.

Gastritis

Mechanism:—On numerous occasions under the fluoroscope I have observed the peristalsis of the duodenum associated with gallbladder disease. In such a case, there is an antiperistalsis which carries the irritating duodenal juices upward into the stomach. I have reproduced this same condition with the morphine drugs and

have observed it in pregnancy, both conditions which are known to simulate the physiological disturbance of biliary tract disease. This regurgitation of duodenal juices frequently sets up a gastritis in the stomach. Often, at times, the regurgitation goes on through the night, resulting in esophagitis, producing the symptoms of heartburn. We have seen cases in which the green bile has actually stained the back teeth of the patient. Many a time they awake in the morning with a brownish discoloration at the back of the tongue. Also, reflexly, on occasions, there is a marked pyloric spasm which I have observed on the operating table in many cases of gall tract disease. On two occasions, the pyloric muscle was so hypertrophied as to produce obstruction and projectile vomiting simulating congenital pyloric stenosis. In these cases it was necessary to do a pyloroplasty.

Symptoms:—The patient complains of gaseous eructation. The belching produces some relief. There is a considerable amount of heart-burn and loss of appetite. There is a feeling of fullness immediately after eating.

Treatment:—During the gallbladder operation, one should stretch the pyloric musculature sufficient to admit two fingers. When the condition is severe it may be necessary to do a pyloroplasty. A bland diet should be given and at times, parenteral administration of liver extract may be necessary.

Cardiac Complications

Through the vagus nerve, reflex disturbances are set up which involve the related organs and at times may involve the heart. This results in a general spasm of the vascular tree. An irritable area on the heart muscle conducive to paroxysmal tachycardia may be activated by this mechanism. For some time paroxysmal tachycardia has been known to be associated with gallbladder disease. Angina pectoris and even coronary thrombosis may be aggravated or precipitated reflexly by impulses arising in a diseased gallbladder. A diseased gallbladder in such cases should be removed if the patient's condition permits.

Nutritional Disturbances

It has long been noted that persons suffering from gall tract disease are vary prone to arthritis of an intractable type. At first it was believed that the gallbladder was a focus of infection. However, it is my belief that the reflex disturbance associated with gallbladder disease resulting in disturbance of digestion, leads to a condition of impaired nutrition and a breaking-down of the joints. The gallbladder, as it lies in the liver bed, is drained by lymphatics which go into the liver substance. Who knows but that there are certain amino acids necessary to the patient's health which this damaged liver fails to produce. I have frequently noted a tendency on the part of patients with long-standing gallbladder disease to suffer from various skin ailments. I can recall at least a half dozen such cases of women in their early sixties with various types of skin rash which clear up promptly after the gallbladder was removed.

Discussion

It is my impression that the far-reaching and detrimental effects of gallbladder disease on the liver, pancreas, stomach, heart, and nutrition in general, is so great as to be explained on a reflex basis rather than from toxins directly absorbed from

the diseased gallbladder. For this reason, we believe that it is important in removing the gallbladder during the dissection of the cystic duct to dissect out freely all the vagus nerve fibres around the duct and to remove them before the cystic duct is clamped. Reports have appeared in the literature of cases termed postcholecystectomy syndrome or biliary dyskinesia in which relief was obtained by removal of the cystic duct. We do not believe that the presence of the cystic duct alone would produce these far-reaching symptoms. It is my considered opinion that the beneficial results reported was a result of removal of small neuromata on the vagus nerve fibres which were tied in with the remaining cystic duct. I have always made it a practice to leave, deliberately, a generous portion of cystic duct so as to avoid stricture of the common bile duct and have seen no harm from this procedure provided the vagus nerve fibres were separately removed.

Summary and Conclusions

In treating gall tract disease, one has to get away from the idea of treating of the single organ. The diseased gallbladder is a focus of impulses which results in the far-reaching disturbances, such as pancreatic edema, duodenal spasm, cholangitis, gastritis, and even cardiac disease. Attention to all these factors is necessary in the treatment of biliary disease. After the removal of the gallbladder, one may be left with a sequela which may require further treatment although the cause has been removed.

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ANESTHESIA FOR GASTROINTESTINAL SURGERY*

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The Department of Anesthesiology has been able to draw certain conclusions in regard to the choice of anesthesia for gastrointestinal surgery from the variety of problems presented by the large volume of patients that have been operated for these conditions at the Boston City Hospital.

Evaluation of Anesthesia Methods

Occasionally, the question is still asked whether spinal or general anesthesia is better for abdominal surgery. The answer is spinal anesthesia. Its reliability, efficiency, and simplicity are the reasons for this choice[1]. It is felt, however, that this answer may not hold true everywhere. There is a great difference between the spinal anesthesia which is practiced in hospitals where it is the main choice for abdominal and lower extremity surgical work, and that practiced in hospitals where spinal anesthesia is only occasionally administered. It is believed that without thorough training and extensive experience in spinal anesthesia, no surgeon or anesthesiologist is in a position to know the best that spinal anesthesia can offer.

Of the various types of spinal anesthesia, the conventional technic employing a single dose of spinal agent is most frequently used. The administration of 100 per cent oxygen is routine. A recent development of this technic is the prolongation of the anesthetic effect. This prolonging effect is produced by the well-controlled use of such potent agents as nupercaine[2] and pontocaine[3], as well as the addition of epinephrine to the injected anesthetic[4]. With one single dose of spinal injection, anesthesia with abdominal relaxation for over two to three hours' duration can be safely accomplished. As a result, this type of single dose spinal anesthesia today, replaces continuous spinal anesthesia in many instances, which, just a few years ago, would have required the latter choice. Nevertheless, continuous spinal anesthesia cannot be dispensed with altogether. It is still the best method for operations of uncertain duration and patients in poor condition. This has been demonstrated in operations lasting from four to eight hours. The adaptability of the fractional dosage of spinal agent to the patient's condition during the course of the operation is an advantage of this method.

The most recent advance in spinal anesthesia technics is segmental spinal[5]. This technic employs a fine ureteral catheter advanced into the subarachnoid space through a special curved tipped spinal needle, so that the tip of the catheter lies in

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*Presented before the Postgraduate Course in Gastrointestinal Surgery of the National Gastroenterological Association, Boston, Mass., 27, 28, 29 October 1949.

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close proximity to those nerve roots which supply the dermatomes at the site of the operation. A small dose of spinal anesthetic agent injected through this catheter will produce a segmental type of anesthesia; that is, it anesthetizes only the segments at the site of the operation, leaving the rest of the body above and below the operative area unanesthetized. This technic, although elaborate and not without dangers, seems to have value in bad-risk patients who are not suitable for other methods which are indicated in such cases, such as local anesthesia and contraindicated for cyclopropane with curare. Another technic is balanced spinal anesthesia, which was developed at the Boston City Hospital in 1936[6]. This is a combination of small dose spinal anesthesia supplemented with general anesthesia, preferably cyclopropane-oxygen, but nitrous oxide-oxygen and ether may be used in low concentrations. The patient is merely carried to the first plane of the third stage anesthesia; in other words, a light sleep, and not a deep anesthesia. The amounts of these anesthetics, if used alone, would be insufficient to produce anesthesia for abdominal surgery. However, when used together, their combined effect gives satisfactory anesthesia with good relaxation. There are little changes in the blood pressure with this technic and the postoperative complications are minimal.

General anesthesia for abdominal surgery has gained impetus by the introduction of curare in anesthesiology[7]. With the addition of curare, adequate abdominal muscular relaxation can be accomplished with cyclopropane or pentothal. Neither of these agents affects the patient's physiology as profoundly as ether. These combinations in our experience have proved to be second choice to spinal anesthesia in abdominal surgery. Since its introduction five years ago, much has been learned about curare and further developments can be expected[8].

Infants and older children undergoing abdominal surgery present a special problem[9]. Ether is most frequently used, insufflated with air or oxygen by means of the Edison vaporizer. An intratracheal tube is employed with the Ayres' T-connector. Another choice for very young children is intratracheal cyclopropane oxygen with carbon dioxide absorption technic. For the older child over five years of age, in selected cases, spinal anesthesia is employed.

In the ensuing discussion, the good-risk, borderline-risk, and poor-risk patients are classified as follows. The good-risk patient is the type who has surgical pathology, but no complicating pathology; the borderline-risk patient has varying degrees of surgical pathology and varying degrees of complicating pathology; the poor-risk patient presents severe surgical pathology and severe complicating pathology.

For the good-risk elective cases undergoing abdominal surgery, spinal anesthesia is generally used. For the low abdominal operation, spinal anesthesia without additional anesthetic is the choice, whereas for upper abdominal surgery, the patients receive spinal anesthesia and then routinely are put to sleep with small amounts of low concentrations of cyclopropane or pentothal and nitrous oxide. This sleep is not a true general anesthesia superimposed on the spinal, but is a hypnosis from which the patient can awake in short order. The reason the hyp-

nosis is indicated for this type of surgery is that the nerve supply to the upper abdominal viscera includes fibres mediated by the vagus and phrenic nerves[10]. Neither of them is affected by properly given spinal anesthesia. That is why patients undergoing gastric or biliary surgery under spinal anesthesia alone may complain of distress in their chest, shoulder blade, or neck at certain times during the operation. This can happen even though the spinal anesthesia is at the proper level and produces complete relaxation. These sensations are best obliterated by a light sleep, because they not only cause suffering to the patient and are disturbing to the surgeon, but often lead to circulatory depression by their reflex effect. The protecting effect of such a light sleep explains why the clinical course of the patients having spinal anesthesia and hypnosis can be maintained more normally than those having spinal anesthesia alone.

In the borderline and the poor-risk elective cases undergoing abdominal surgery, balanced spinal anesthesia is one of the most suitable methods. Since the systemic effect of the low doses used in this technic is apparently not cumulative, it does not affect the general condition of the patients to any appreciable extent.

An important consideration in the management of these patients during the preoperative period is the building up of their general condition: With proper measures that aim to treat their complicating pathology (for example, digitalization of the cardiac patient) and to correct their abnormal physiology (for example, parenteral feeding in inanition) their reserve strength should be built up to its peak, enabling them to cope with the operation[11].

The evaluation of these patients prior to the operation is of great importance. The clinical judgment and experience of the anesthesiologist will enable him to evaluate the patient properly, and choose from the many available anesthetic methods, the one which is best suited to the individual patient. To sum up the available methods: balanced spinal anesthesia; single dose, continuous, and segmental spinal anesthesia; and various combinations such as local with or without curare, and intratracheal cyclopropane with curare. The administration of high oxygen concentrations throughout all anesthesias and the proper administration of fluid therapy is of the greatest importance in this group.

For intrathoracic operations, as esophagectomy, or for operations that employ the thoracoabdominal approach, as sub-total gastrectomy, endotracheal anesthesia is mandatory. Ether-oxygen is preferred as the main anesthetic agent for these procedures because it provides an even maintenance and because it does not seem to affect adversely the general condition of the patient, who, for the most part of the operation, need not be deeply anesthetized. The endotracheal technic enables the anesthesiologist to control the collapse or expansion of the left lung in the case of the widely opened pleural cavity[12]. Cooperation between the surgeon and the anesthetist is of great importance in these operations, especially at the time of opening and closing of the pleura, and during routine endotracheal catheter aspirations. Similarly, cooperation is very important when the surgeon accidentally opens the right pleural cavity during these operations with the left pleural cavity already open. If this happens, irreversible complications can be prevented by the

surgeon promptly notifying the anesthesiologist and taking other measures that will enable the latter to keep the lungs expanded with positive pressure[12].

In the consideration of the good risk emergency cases, the great majority of gastrointestinal surgical procedures, (such as appendectomy, suturing of perforated peptic ulcer, and operations for acute intestinal obstruction), in patients whose general condition is not markedly impaired can be carried out successfully under spinal anesthesia. Again it is emphasized that the knowledge, ability, and experience of the anesthesiologist in handling these cases with spinal anesthesia is a decisive factor in making this choice safe and successful. The use of carefully selected doses of spinal anesthetic agent, together with the proper administration of fluid therapy, and administrations of 100 per cent oxygen, results in a uniformly favorable clinical course. A definite advantage of this choice is the safety against the hazard of aspiration of vomitus in the emergency case.

In the care of the bad-risk emergency cases, in those patients where hemorrhage, injury, or advanced toxicity leads to shock, the first consideration is to correct this condition by adequate therapy[13]. Even when this is accomplished, and the patient's condition has improved to the point where operation is to be performed, he may still be in a state bordering on shock. For this type of patient, local anesthesia is preferable. Unfortunately, this choice often leads to unsatisfactory operating conditions.

Spinal anesthesia is contraindicated for this type of patient, because the circulatory changes produced by the spinal anesthetic aggravate the already existing pathology. The circulation of these patients is characterized by the reduction of the effective blood volume[14]. Spinal anesthesia producing vasodilation in the splanchnic area and reducing the venous return to the heart, duplicates this circulatory disturbance[15].

Of the general anesthetics ether is contraindicated for these patients, because of its deleterious effect on vasomotion[16]. This phenomenon, which has great significance in the pathological physiology of shock is an important peripheral compensatory mechanism[17,18,19]. Vasomotion is described as "intermittent periodic changes in the calibre of the terminal arterioles and their precapillary side branches, and is an activity which regulates the distribution of blood through the capillary bed". Ether has a dampening effect on vasomotion by producing an early appearance of a vasodepressor material in the blood.

The effect of pentothal on vasomotion is uncertain[16]. In the very early shock syndrome its judicious use in small doses may produce favorable results, but with use of larger doses its effect is depressant, quite similar to that of ether. The transition from one type of reaction to the other is unpredictable. Therefore, the use of pentothal is not recommended in these cases.

The effect of cyclopropane on vasomotion is the opposite of that of ether[16]. The absence of impairment of the vasomotor adjustment mechanism, and the inhibition of the appearance of vasodepressor material in the blood, explain why the circulatory dynamics during cyclopropane anesthesia in these cases most closely resemble those seen in unanesthetized patients. Cyclopropane, therefore,

is the general anesthetic of choice for the patient close to shock. However, it may not produce complete abdominal relaxation. This is obtained by the additional administration of curare. This does not seem to affect the circulation to any appreciable extent if the proper dosage of curare is used, but produces ideal working conditions for the surgeon[1]. The gratifying results with cyclopropane-curare combination in a large series of subtotal gastrectomies performed on patients with uncontrollable gastric hemorrhage, and similar results in a large number of cases with severe injury or advanced toxicity, amply illustrate the correctness of this choice.

A major consideration in emergency gastrointestinal surgery is the possibility of aspiration of vomitus or regurgitated material. When spinal or local anesthesia are used, the safeguard against aspiration of vomitus is the conscious state of the patient. However, an emergency bad-risk patient under a general anesthesia such as cyclopropane-oxygen with curare is in real danger from this complication. To overcome this, the routine use of an endotracheal tube equipped with an inflatable cuff is recommended. The topical anesthesia of the throat with pontocaine given prior to the induction facilitates the intubation. After the cuff on the intratracheal tube is inflated, the patient will be safe from the danger of aspiration. Patients in this group should be intubated as soon as possible in early cyclopropane induction.

To illustrate some of the points emphasized in this presentation, a brief review is given of the anesthesias for the operations that have been televised for the past three days*. Of these operations, eleven were performed through the abdominal and one through the transthoracic approach. For the abdominal operations, seven different methods of spinal anesthesia were used, due to the marked variation in the condition of the patients and the indicated types of surgical procedures. Endotracheal anesthesia was administered for the transthoracic operation. Two of the cases, which were low abdominal operations, did not receive any anesthetic other than spinal; the other nine cases, all upper abdominal operations, were anesthetized with spinal anesthesia and kept in light hypnosis with small amounts of pentothal-sodium and nitrous oxide-oxygen. We have seen the uniformly relaxed and quiet operative field throughout these operations. With the exception of two instances of mild, transitory hypotension for brief periods of time, all the patients maintained normal blood pressure with negligible variations throughout all of these procedures.

Of this series, two illustrative cases are mentioned.

Case 9:—A sixty-eight year old woman had an obstructing tumor in the ascending colon. Prior to admission she lost 30 pounds; she had poorly functioning liver and her Hg. was 10 gm. The operation was a right colectomy and lasted 3 hours and 25 minutes. A single dose spinal anesthesia was given, using 7½ mg. of nupercaine with ½ c.c. of adrenalin 1:1000 and mixed with a 10 per cent glucose solution. The patient was kept asleep throughout the operation with pento-

*This paper was presented on the afternoon of the third day of the Postgraduate Course in Gastrointestinal Surgery at the Boston City Hospital on 27, 28, 29 October 1949. As part of the course, a series of gastrointestinal operations were performed and shown by television.

thal and nitrous oxide-oxygen. The total amount of pentothal given over a period of 3½ hours was 13 c.c. of 2½ per cent solution, less than ⅓ of a gram. The nitrous oxide-oxygen concentrations were 50 per cent each. Throughout the operation the relaxation was perfect and the patient maintained her normal blood pressure with negligible variations at all times.

Case 10:—A seventy-six year old man had a chronic duodenal ulcer. He was markedly debilitated and had a Hg. of 11 gm. A subtotal gastrectomy was performed and lasted 4 hours and 30 minutes. The total anesthesia time was 5 hours. Segmental spinal anesthesia was used, in this case employing a mixture of pontocaine, glucose, and distilled water. The total amount of spinal anesthetic given was 8 mg. of pontocaine. This patient was kept asleep by the same method as was used in Case 9 with pentothal and nitrous oxide-oxygen. The total amount of pentothal was 15 c.c. of the 2½ per cent solution, slightly over ⅓ of a gram. Both relaxation and clinical course were as satisfactory in this case as in the previous one.

Case 12:—A seventy-two year old man had an obstructing tumor in the esophagus. He is a very poor risk patient in a state of extreme inanition, weighing 70 pounds. A mixture of cyclopropane administered endotracheally with ether with high concentrations of oxygen was used. The patient showed an uneventful clinical course. He went through the 3 hours, 35 minutes, procedure in the same very satisfactory condition. The postanesthetic recovery was uneventful.

In conclusion, it may be said that the choice and management of anesthesia plays an important role in accomplishing the best possible results in gastrointestinal surgery. It is felt, that with the better preparation of the patient for surgery, with the proper choice of anesthesia, with the best possible anesthetic management of the patient before, during, and after the operation, and with the simultaneous physiologic application of inhalation and fluid therapy during the same periods, the results attainable today in gastrointestinal surgery, show greater improvements over those of a very few years ago.

Summary

Various methods of anesthesia for gastrointestinal surgery are presented; recent advances in spinal and general anesthesia are mentioned; the choice of anesthesia is discussed for elective and emergency gastrointestinal surgery, distinction being made between that chosen for the good risk and that for the bad risk patients. The physiological basis for use of certain agents is pointed out, and the problem of aspiration of gastric contents is considered.

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COMPLICATIONS OF ACUTE APPENDICITIS*

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This paper is a review of all the cases of acute appendicitis treated at the Boston City Hospital during the first six months of 1949, with particular attention to the nature and incidence of complications of the disease. The complications are, of course, the only serious part of it. As stated in Christopher's well-known textbook of surgery[1], "there are no complications of acute appendicitis as long as the infection is within the appendix, but once the organisms reach the peritoneal surface, serious and far-reaching complications may develop".

In 1933, Dr. Irving J. Walker[2] of this hospital reported that in the four year period, 1927-30, the mortality for 2,106 cases of appendicitis treated at the Boston City Hospital was 5.8 per cent. This included uncomplicated cases as well as those with rupture, abscess and peritonitis. Rogers and Faxon[3] reported that in 671 cases of appendicitis complicated by peritonitis treated at the Massachusetts General Hospital between 1929 and 1940, the mortality was 12.97 per cent.

TABLE I

PATIENTS OPERATED ON WITH PREOPERATIVE DIAGNOSIS OF APPENDICITIS
(JANUARY 1-JUNE 30, 1949)

Acutely Inflamed Appendix Found	201
Healed Appendicitis	38
Missed Diagnoses	45
Total	284

It was felt that with the recent development of greatly improved methods of treatment, particularly chemotherapy and antibiotics, a review of the present cases of acute appendicitis at this hospital might be both interesting and instructive.

To determine the present situation at the Boston City Hospital with regard to this disease, the records of all patients operated on with a preoperative diagnosis of appendicitis during the first six months of the year 1949, were carefully reviewed. There were 291 such cases. Seven of the records were not available because they were not yet completed, but the remaining 284 were studied statistically.

In each case, the operative note and pathological report were carefully considered and it was found that 201 of the 284 cases had shown definite acute inflammation of the appendix at the time of operation. The remaining eighty-three (29 per cent), (see Table I), showed thirty-eight cases of "healed appendicitis". Our pathological department makes a diagnosis of "healed appendicitis" in cases where microscopic examination of the appendix shows evidence of previous inflammation. Many of these cases had evidently been operated on in between acute

*Presented before the Postgraduate Course in Gastrointestinal Surgery of the National Gastroenterological Association, Boston, Mass., 27, 28, 29 October 1949.

attacks of appendicitis. However, there were forty-five cases where the preoperative diagnosis was definitely incorrect. The most common missed diagnosis, (see Table II), was mesenteric adenitis. As we all know, this condition is at times practically impossible to distinguish from acute appendicitis. The other missed diagnoses seemed to be mostly the usual ones found in textbooks of surgery, such as ruptured corpus hemorrhagicum, Meckel's diverticulitis, pelvic inflammation, etc., but there were two unusual ones. One was a case of ruptured right deep epigastric vein which had evidently occurred during a fit of severe coughing, and the other unusual case was that of a dermoid tumor of the small intestine.

Henceforth in this paper we shall consider only these 201 cases definitely shown at operation to have been suffering from acutely inflamed appendices.

Walker[2] reported that in the four year period, 1927-30, appendicitis in this hospital occurred 61 per cent in males and 39 per cent in females. For the first six months of this year, 1949, there was a slightly higher proportion of males, 65 per cent to 35 per cent females. In other words, nearly two-thirds of the cases of acute

TABLE II

45 Missed Diagnoses

(16% of 284 Cases Diagnosed Preoperatively As Appendicitis)

	No.	%
Mesenteric Adenitis	27	60
Ruptured Corpus Hemorrhagicum	5	11
Ovarian Cyst	3	7
Meckel's Diverticulitis	2	4.4
Pelvic Inflammation	2	4.4
Pneumococcus Peritonitis	2	4.4
Ruptured R. Deep Epigastric Vein	1	2.2
Dermoid Tumor of Small Intestine	1	2.2
R. Ureteral Calculus	1	2.2
Perforated Peptic Ulcer	1	2.2
	45	100.0

inflammation of the appendix operated on in this hospital during the first part of this year were found to be in males.

A comparison was made in Table III between the incidence of appendicitis according to age as found by Walker[2] at the Boston City Hospital, 1927-1930, and the same during the first six months of this year. The age incidence in the two periods was found to be approximately similar except that there appeared to be a slight increase in the number of middle-aged and elderly patients during 1949. This may well have been due, at least in part, to longer life expectancy of the general population now as compared to twenty years ago.

An attempt was made to determine the present incidence of preoperative complications. The most important of these seemed to be perforation, abscess formation, and peritonitis. All cases of acute inflammation of the appendix must, of course, if at all extensive, produce some degree of visceral peritonitis and the exact degree is sometimes very difficult to determine at operation. Therefore, only cases noted at operation to have had generalized peritonitis were recorded as such in our table (Table IV). There were fifty-one cases of acute appendicitis with

perforation, 25 per cent or ¼ of the total number of cases of acute appendicitis. However, only 22 cases (11 per cent) had appendiceal abscesses, and only 8 cases (4 per cent) had gone on to generalized peritonitis. It was assumed in cases of abscess and generalized peritonitis that there had been a perforation of the appendix.

The cases studied were too recent to be able to determine the long-term postoperative complications, such as late intestinal obstruction, which may occur years later, and late wound hernia. However, by studying all the progress notes

TABLE III

INCIDENCE OF ACUTE APPENDICITIS ACCORDING TO AGE

	1st 6 months 1949		2106 Cases, 1927-1930 (Walker)
	No. Cases	%	%
0–9	33	16	19
10–19	88	44	44
20–29	30	15	21
30–39	14	7	8
40–49	15	7	5
50–59	11	5	2
60–69	8	4	1
70–79	0	0	0.05 (1 pt.)
80–89	1	1	0.05 (1 pt.)

and discharge notes, it was possible to determine the incidence of immediate postoperative complications.

These are shown in Table V. Major wound sepsis occurred in 21 cases and minor wound sepsis was noted in only four cases, a total of twenty-five cases, or 12 per cent of 201 cases. Four of these cases developed sufficient deep major sepsis to require subsequent incision and drainage while still in the hospital. Two cases developed pelvic abscesses after operation, although both had had intraperitoneal drains inserted. Both ruptured the abscess spontaneously into the lower bowel.

TABLE IV

PREOPERATIVE COMPLICATIONS OF ACUTE APPENDICITIS (201 CASES)

	No. Cases	%
Perforation	51	25
Abscess	22	11
Generalized Peritonitis	8	4

There were three recorded cases of postoperative pneumonia and three of immediate wound hernia. There was only one wound dehiscence. This was immediately resutured, but eventually developed a hernia in the wound. This incisional hernia was repaired two and one-half months later.

There was only one case of postoperative phlebitis of the legs, noted eleven days after operation in a woman of 54. It seems reasonable to suppose that the policy of getting the patients out of bed within a day or two of operation, begun only in recent years, has markedly reduced the incidence of postoperative phlebitis.

There was one case of intraperitoneal hematoma. It was incised and drained twelve days after operation. There was one case of septicemia.

There were no cases in this series of 201 acutely inflamed appendices of either pylephlebitis or subphrenic abscess. No pulmonary embolism was noted in any case.

There were only two deaths in our series, an incidence of very slightly less than 1 per cent. One was a little girl, age 3 years, who had been given eight separate enemas at home in an ill-advised attempt to relieve abdominal pain. Six

TABLE V

Immediate Postoperative Complications of Acute Appendicitis (201 Cases)

	No.	%
Wound Sepsis	25	12.5
Pneumonia	3	1.5
Wound Hernia	3	1.5
Pelvic Abscess	2	1.0
Intraperitoneal Hematoma	1	0.5
Wound Dehiscence	1	0.5
Intestinal Obstruction	1	0.5
Phlebitis	1	0.5
Septicemia	1	0.5
Death	2	1.0 (or 0.995)

enemas had been given the day before admission and two on the day of admission. She was noted to have had a convulsion as she was being admitted on the accident floor of this hospital. A ruptured appendix was found at operation, with generalized peritonitis. In spite of penicillin, streptomycin and sulfadiazine, she developed pneumonia and septicemia and died nine days after admission.

The second death occurred in an old woman of 84 who was operated on for a ruptured appendix and generalized peritonitis. In spite of penicillin and streptomycin, she died on the twenty-eighth hospital day of pneumonia, uremia and major wound sepsis.

TABLE VI

Average Number Hospital Days

Acute Appendicitis (uncomplicated)	10
With Perforation	16
With Abscess	22
With Gen. Peritonitis	21

The morbidity as shown by the average number of hospital days appears in Table VI. The cases of uncomplicated, acutely inflamed appendices averaged ten days in the hospital. With perforation, they averaged sixteen days and with abscess formation, twenty-two days. The eight cases found to have had generalized peritonitis averaged twenty-one days in the hospital. As stated above, there were two deaths among the eight cases of generalized peritonitis.

With five separate general surgical services in this hospital, methods of treatment, particularly as to the choice of drugs, may vary slightly. Table VII shows

what chemotherapeutic and antibiotic drugs were given in the various types of appendicitis.

Penicillin was given in varying amounts, a good standard dosage seems to be 100,000 to 200,000 units intramuscularly every three hours. Eighty-seven per cent of the cases without perforation were given penicillin as were all the cases of perforation, abscess or generalized peritonitis. It seems a little more effective to start the administration of penicillin preoperatively if possible. We feel that penicillin given with an agent to slow down its absorption should never be administered in these cases, to combat serious soiling of the peritoneal cavity.

Streptomycin was given in many of the sickest cases suffering from perforation, abscess or peritonitis. The usual dosage for an adult was 1.0 grams intramuscularly followed by 0.5 grams intramuscularly every six hours for a total of 10 grams. As shown in Table VII, few of the cases without perforation were given streptomycin, but about half of the cases with perforation and most of those with abscess or generalized peritonitis were given the benefit of this drug. Dr. Maxwell Finland[4] of this hospital feels that more of these cases with peritoneal soiling could have been given streptomycin with benefit.

TABLE VII

Number of Cases Treated With Chemotherapeutics and Antibiotics

	Penicillin	Streptomycin	Sulfadiazine
Acute Appendicitis			
Without Perforation	130 (87%)	8 (5%)	14 (9%)
With Perforation	51 (100%)	25 (49%)	20 (39%)
With Abscess	22 (100%)	15 (68%)	7 (32%)
With Generalized Peritonitis	8 (100%)	6 (75%)	4 (50%)

Sulfadiazine was also employed in many cases, either as sulfadiazine itself by mouth or as sodium sulfadiazine intravenously. By mouth, sulfadiazine was usually given with an initial dose of 2 grams followed by one gram every four hours. By vein, sodium sulfadiazine was given usually in one dose of 2.5 grams to 5.0 grams, diluted in large amounts of normal saline solution at the time of operation. In several cases, both intravenous sodium sulfadiazine and a course of sulfadiazine by mouth were employed. The patient should, of course, be hydrated adequately before sulfonamides are given. In very ill cases of ruptured appendix, the patient should probably be given the benefit of all three drugs, penicillin, streptomycin and sulfadiazine.

Dr. Finland[4] has informed us that aureomycin given intravenously in cases of peritonitis will produce great benefit, but is a very irritating substance in the subcutaneous tissues unless venepuncture is perfectly done. We have as yet had little experience with this drug on the surgical services at the Boston City Hospital.

The types of incisions used were several. The right lower rectus splitting incision was used in more than half the cases. This is, of course, one of the simplest and fastest incisions for an appendectomy. However, when the surgeon wishes to explore the pelvis, as in a female where pelvic inflammatory disease is a possibility, retracting the rectus muscle laterally certainly gives a much better exposure.

In cases where exploration is not indicated, and an acutely inflamed appendix or an appendix abscess is thought to lie lateral to the cecum, a McBurney incision seems definitely safer and better. There were only nineteen McBurney incisions in the 201 cases. Six of these were drained. Possibly, in retrospect, it would have been better to have used more McBurney incisions, particularly for the drainage of lateral appendix abscesses.

A brief study was made of the incidence of drainage of incisions in these 201 appendectomies for acutely inflamed appendices (see Table VIII). In thirty-six cases or 18 per cent, the peritoneal cavity was drained. However, only fourteen out of the twenty-two appendix abscesses were drained. The other drains were inserted for peritoneal soiling without definite abscess formation. In twelve cases or 6 per cent, only the abdominal wall was drained. There were five cases in which the peritoneal cavity was drained through a stab wound. Possibly this might not have been necessary had a McBurney incision been used. However, as is well known, the location of an appendix abscess may be very difficult to determine before operation.

TABLE VIII

Incidence of Drainage in 201 Operations for Appendicitis, Acute

	No.	%
Peritoneal Cavity	36	18
Abdominal Wall Only	12	6
(Both Perit. Cav. and Abdominal Wall 4)		
Stab Wound to Abdominal Cavity	5	2.5

In retrospect, it might have been better to draain more of the abdominal incisions extraperitoneally to avoid the wound sepsis which occurred in 12 per cent of the cases. However, at the Boston City Hospital we try to be very careful to use skin towels. We also try to make every effort to avoid soiling the subcutaneous tissues in the abdominal wall with contaminated abdominal contents, as from an appendix abscess or from an acutely inflamed appendix.

In conclusion, a study was made of all cases operated on with a preoperative diagnosis of appendicitis at the Boston City Hospital during the first six months of 1949, with particular attention to complications of this disease.

Summary

1. Of 284 cases preoperatively diagnosed as acute appendicitis, 201 or 71 per cent were found to have acutely inflamed appendices.

2. Twenty-five per cent of these 201 cases showed perforation of the appendix.

3. Eleven per cent of the 201 cases showed an appendix abscess.

4. Four per cent of the 201 cases showed generalized peritonitis.

5. The commonest postoperative complication was wound sepsis, occurring in 12 per cent. Other postoperative complications occurred only in very small percentages of the patients.

6. Penicillin was used in 100 per cent of the cases of perforated appendix. Streptomycin and sulfadiazine were also used in a large percentage of the sickest cases.

7. There were only two deaths in the entire series of 201 cases, a mortality of slightly less than 1 per cent.

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FASTING ACHLORHYDRIA AND HYPOCHLORHYDRIA PRODUCED BY PROTEIN HYDROLYSATE THERAPY OF PEPTIC ULCER*

A Preliminary Report

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Of the several factors necessary for prompt healing of peptic ulcer lesions and for prevention of recurrence, the reduction of the level of gastric acidity, particularly fasting (night) acidity has been considered primary[1]. No reduction in the fasting (night) gastric acidity has been noted in ulcer patients under medical management with various modifications of the Sippy regime nor does the healing of the ulcer per se seem to cause any appreciable reduction of the fasting acidity[2,3,4]. This failure to achieve prolonged reduction in gastric acidity by ordinary medical means led to the development of surgical procedures, particularly vagotomy, which are considered to be successful only when gastric acidity is eliminated.

The efficacy of protein hydrolysates both in the control of the acute symptoms of peptic ulcer and in the long term management without requiring hospitalization first reported by Co Tui et al[5], has been attested to by many workers[6-18]. However, since this treatment is only 4 years old, neither the mechanism of its action, nor the collateral phenomena attending its use have been worked out.

The present preliminary report records the achievement of fasting anacidity and hypoacidity in eight consecutive cases of duodenal ulcer after four to five weeks of protein hydrolysate therapy. This beneficial pharmacologic action of hydrolysates on gastric acidity if borne out by future studies, would show it to be in effect a "medical vagotomy".

Clinical Material

These were random cases of chronic duodenal ulcer, all males with histories of 2, 10, 10, 10, 13, 15, 15 and 20 years duration respectively, repeatedly proven on x-ray, but none of whom showed any evidence of gastric retention or other complications. All of these patients had received modified Sippy or one of the other modifications of conventional therapy of varying degrees of intensity for many years.

Method

The course of treatment was substantially that outlined by Co Tui[5] with the exception that hourly feedings were used instead of 2-hourly feedings.

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The patients were given an amount of casein hydrolysate (Edamin) equivalent to 0.6 gram of nitrogen per kilo body weight. The caloric value was made up to 50 calories per kilo by the addition of Dexin. These two substances were given as separate solutions each dissolved in a quart of water, an aliquot portion being taken each hour for sixteen hours, from 8:00 A.M. to 11:00 P.M. For the first two weeks, nothing else (foods or medication) was taken by mouth, except water. At the end of this period, and for the next two weeks, the patient was allowed to substitute for three of the hydrolysate feedings, meals consisting of any of the following five foodstuffs: milk, boiled eggs, boiled chicken, toasted white bread or cooked cereal (oatmeal, farina, or wheatena).

Fasting acidity was determined preceding the institution of therapy and then again at the end of the four-week period, using Topfer's reagent for free acid and phenolpthalein for total acidity. To eliminate any effect due to the passage of the tube, three specimens were drawn at fifteen minute intervals and an average value taken.

The study was modified in Patient 1 by extending therapy for a fifth week after which another determination of fasting acidity was done. The patient was then taken off treatment and allowed to resume his normal diet for a week after which a gastric analysis was again performed.

Patient 3 was continued on therapy for nine weeks, repeat determinations being done at the 6th and 9th weeks.

Results

The results obtained are shown in Table I. It will be seen that in two patients the fasting free acid was reduced to zero, in two other patients, it was reduced to a very low level (5 units and 11 units respectively). In the other four patients, it was reduced by approximately forty per cent. The average free acidity of the group was reduced from a level of 60 units initially to a level of 18 units after therapy.

Discussion

While the normal individual only produces a small amount of secretion of low acidity during the night[1], there is a characteristic tendency for duodenal ulcer patients to secrete highly acid gastric juice. This nocturnal secretion is thought to be vagal in origin[19]. Dragstedt and co-workers[20,21,22] concluded similarly that fasting peptic ulcer patients have an excessive continuous secretion of gastric juice of higher acid content than normal and that this hyperchlórhydria operates to produce the ulcer and hinder healing. The fasting gastric acidity is therefore of utmost importance in diagnosis, prognosis and therapeusis.

Winkelstein[1], on the basis of 4 cases studied, states that after three weeks of drip therapy, the curve for night acidity declined markedly, and explains partially, the efficacy of drip therapy on this decline in night acidity. The mechanism for the decline of the acidity, he feels, is a breaking of the conditioned reflex (nervous) phase of gastric secretion.

The only relevant information on the fasting acidity in the course of protein hydrolysate therapy for peptic ulcer is the statement of Hodges[10] that the acid

secretory response of the patients to a test meal of oatmeal gruel immediately before and after two weeks of treatment, was decreased in six patients, increased in two and unchanged in two. However, Hoelzel in 1926[23] in a study on a single subject, reported that an excessively high protein intake caused a decrease in the acidity of the fasting gastric secretion.

From the findings in the present study and from reports in the literature, there appear to be three ways in which protein hydrolysates affect the gastric acidity of peptic ulcer patients. In the first place, there is direct chemical neutralization—which has been reported by Levy[24] and by Co Tui[5]. Secondly, there seems to be a rebound phenomenon, which has been reported by Winkelstein[4] and by Rossien[12]. The effect reported in this paper constitutes the third effect. While the mechanism involved in the first effect is obviously that of direct chemical neutralization without any physiological intermediation on the part of the patient, the mechanism involved in the last two effects are not clear, but are perhaps mediated physiologically. As has been stated, the healing of the peptic ulcer per se, which is presumably taking place at this time, has not been found to reduce the fasting acidity[2,3,4].

TABLE I

GASTRIC ACIDITY VALUES BEFORE AND FOLLOWING PROTEIN HYDROLYSATE TREATMENT

Patient		1	2	3	4	5	6	7	8	Aver.
Before Therapy	F.A.	78°	57°	72°	82°	58°	32°	39°	62°	60°
	T.A.	89°	79°	90°	99°	81°	52°	58°	90°	80°
After 4 weeks Therapy	F.A.	11°	0°	42°	0°	30°	5°	22°	36°	18°
	T.A.	25°	4½°	54°	9°	62°	17°	40°	61°	34°

F.A. – Free Acid T.A. – Total Acid

The work of Crider and Walker[25] may have a bearing in this connection. These authors found that intravenous injection of protein hydrolysates causes not only a change in the motility of the stomach, but also a reduction in both the gastric hydrochloric acid and pepsin. It has been suggested[26] that this train of phenomena are due to hyperaminoacidemia, and that since hyperaminoacidemia is also present following the oral administration of protein hydrolysates, the reduction in the hydrochloric acid level found in these 8 patients might well be on the same basis.

The physiologic mechanism whereby hyperaminoacidemia reduces gastric acidity is unknown. There are, however, certain clinical observations which, when integrated, suggest a pattern of bodily response depending on a counterrelationship between adrenal cortical activity and histamine or related "H" substance activity. This counteraction is evidenced by the positive correlation, on the one hand, between the incidence of histamine induced or histamine aggravated pathologic conditions, and the incidence of peptic ulcer, and the negative correlation, on

the other hand, between the incidence of conditions with high antihistamine titer and the incidence of peptic ulcer.

Thus patients and families with allergic manifestations show a fairly high incidence of peptic ulcer[27], whereas in pregnancy with its extremely low incidence

TABLE II
GASTRIC ACIDITY IN PATIENT 1 AFTER PROTEIN HYDROLYSATE TREATMENT AND FOLLOWING RESUMPTION OF ORDINARY DIET

After 4 weeks Therapy	F.A.	11°
	T.A.	25°
Therapy discontinued 1 week	F.A.	36°
	T.A.	46°

F.A. – Free Acid T.A. – Total Acid

of ulcer[28], there is a progressively increased histaminolytic titer in the blood[29] in conjunction with a marked increase in adrenal steroid output. Further corroboration is drawn from the production of acute ulceration of the gastrointestinal tract (Curling's ulcer[30]) in severe burns which are associated with high titers of "H" substance, and destructive lesions of the adrenal cortex[31,32].

TABLE III
CHANGE IN GASTRIC ACIDITY IN PATIENT 1 AFTER PROLONGED PROTEIN HYDROLYSATE TREATMENT

Before therapy	F.A.	72°
	T.A.	90°
After 4 weeks	F.A.	42°
	T.A.	54°
After 6 weeks	F.A.	14°
	T.A.	37°
After 9 weeks	F.A.	15°
	T.A.	33°

F.A.—Free Acid T.A.—Total Acid

To explain these observations, the theory is tentatively postulated[33,34] that the development of peptic ulcer (and perhaps other psychosomatic disorders) is based on an insufficient adrenal cortical response to stress relative to another body mechanism simultaneously elicited by the same stress situation, this other body mechanism being characterized by elevation of histamine or other "H" substance titer. The etiologic role of stress situations such as cold, infection and emotional excitement in the development and recurrence of peptic ulcer could then be explained as due to a dysequilibrium between these two responses characterized by a relative inadequacy of the adrenal response.

According to this hypothesis, hyperproteinization exerts its effect by shifting the equilibrium to increased adrenal response. This interpretation gains partial support from the findings of Moya et al[32] that "under certain conditions, when adrenal cortical growth is stimulated beyond normal, high protein diets further augment corticotrophin response either by increased adrenocorticotrophic hormone production or by eliciting secretion of some synergistic hypophyseal principle".

Although at present still nebulous, this view of the pathogenesis of peptic ulcer merits further exploration and if substantiated, would establish the link between the psychic and somatic aspects of the disease.

But whatever the physiologic basis, this demonstrated prolonged reduction of fasting acidity after protein hydrolysate therapy, must have a beneficial effect both on the healing of the ulcer and on the prevention of relapses. Patient 1 suggests that this reduction may not be permanent after the discontinuation of the treatment. It will be necessary in further work to determine among other things how permanent this effect is after discontinuation of hydrolysates and if possible what its influence is on the incidence of relapses.

Summary and Conclusions

The long-term effect of substitution of protein hydrolysate and dexin for the normal diet in peptic ulcer patients is a marked reduction of fasting gastric acidity.

This reduction in fasting acidity is probably an adrenal cortex mediated response based on increase in the adaptive mechanism as a result of prolonged hyperproteinization.

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COLITIS GRAVIS

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The term *colitis gravis* here refers to the disease which has also been designated as chronic ulcerative colitis or purulent colitis, and in cases where the process is localized entirely in the rectum, ulcerative or purulent proctitis. In our opinion the designation *colitis gravis* is the most adequate, as the course of the disease is in many cases characterized by periods of improvement and deterioration, with or without ulcerations or purulent discharge. Time after time inspection of the mucous membrane or radiography shows that the patient *has* a grave colitis, although in some instances there are ulcers, in others none, and in many cases the disease never reaches the ulcerative stage. The term *colitis gravis* seems therefore to be more appropriate and to cover the picture more adequately than "ulcerative colitis".

The disease is not uncommon in a medical department. For example it may be mentioned that the Falun hospital (the central hospital in Dalcarlia, a reception area with a population of about 250,000) from 1944 to the autumn of 1947, inclusive, received 37 patients who were treated on 65 different occasions, which is approximately 1.2 per cent of the total number of patients admitted during that period. A brief survey of the results of the treatment up to date will be given later.

The nature of the condition is still frequently misinterpreted by the physician, although less often now, because the complaint in its earlier stages cannot be diagnosed without proctoscopic examination. Some cases have therefore had no adequate treatment for considerable periods, on the diagnosis of chronic colitis, gastric diarrhea or constipation diarrhea. Nor can the diagnosis be made from radiographs in the early stages, as the disease generally begins in the rectum as a severe proctitis and the changes in the rest of the colon may be only slight for a considerable period. Not even ulcers of the rectum appear clearly in the radiograph, and thus the reports of this examination at an early stage may be misleading.

The etiology of the disease is still very unclear. Most authors have supported the theory of a bacterial origin. A rather remarkable fact is that the only form of acute ulcerative colitis, dysentery, (amebic as well as bacteriogenic), hardly ever gives rise to chronic ulcerative colitis. Many authors have considered streptococci to be the cause, and the viridans group has been particularly mentioned in this connection. It is a fact that abundant cocci may, in most cases, be cultivated from feces, but as pointed out by Svartz and others, these are mostly enterococci. Not even Svartz, however, who has carried out therapeutic experiments with vaccine and sera against this enterococcal infection, considers that these bacteria have been proved to be the primary cause. For the present it may be considered probable that this abnormal intestinal flora has some bearing on the disease especially as it can be demonstrated that the enterococci decrease with the improvement of the condition, and increase on relapse. But there are also many cases of

colitis gravis in which nothing abnormal may be demonstrated in the intestinal flora.

B. pyocyaneus, B. paracoli, the Welch-Fraenkel B. emphysematosus and certain fungi have been discussed in this connection, but these theories may be discarded without further consideration. It is clear that the disease has nothing to do with tuberculosis, partly as the localization in tuberculous colitis is quite the opposite to that in common ulcerative colitis.

Many authors consider that the disease is allergic in origin. With regard to this interesting possibility, it may be said briefly that it lacks evidence in the symptomatology.

Vitamins are doubtless an important factor in the disease but it is evident that it cannot be caused by the lack of any vitamin known at present. Symptoms of avitaminosis, however, may in some cases appear during the course of the disease. This question will be discussed later. Vitamins, which in severe cases should be given parenterally, cure avitaminosis and help to improve the general condition.

Pathogenesis:—On histologic examination subepithelial infiltrates of mainly lymphoid cells are observed in the preparations. The cells on the surface of the ulcers are multinuclear, and formation of mucus may be observed. The cell infiltration affects the nutrition of the mucous membrane. In advanced cases the infiltration extends far down into the submucosa, or deeper, where abscesses may appear.

The onset of the disease is seldom acute. The first symptoms are usually that the stools during one or several periods become more frequent and looser than normally. The symptoms are gradually aggravated with abnormally violent straining at stools, even actual tenesmus and mucus and blood are passed with the feces. In many cases the condition deteriorates in connection with an acute intestinal infection, "gastric influenza". A patient with continuous symptoms has, as a rule, a history of several such periods and is often constipated in the intervals. In more advanced cases the stools become more frequent, six to eight per day and more, and they become looser with increased passage of mucus and blood. At this stage the diagnosis is already generally clear from the case history. There is severe and imperious tenesmus where proctitis predominates. The patient has usually one to two nightly evacuations and one or two in the morning after waking. A marked gastrocolic reflex is usually present. Colicky spasms occur higher up in the colon, but are not the rule. Severe hemorrhages are not usual.

The general condition is usually surprisingly good at fairly advanced stages, even when the patients complain of incapacitating fatigue and diarrhea. The continuous loss of small quantities of blood gradually causes sideropenia with pallor and anemia. Emaciation occurs only at a fairly late stage. In the most severe cases there is also fever, sometimes accompanied by chills and sudden rises in temperature, which indicates the presence of submucous abscesses, generally discharging per rectum with a drop in temperature. The sedimentation rate, which

is usually normal, and the leucocyte count, show a rise when the processes are deep-going. Tachycardia, also without fever, is present in the most severe cases.

The most important means of diagnosis is the proctoscope. At the early stages, examination of the rectum shows redness, edemas and usually slight hemorrhages of the mucous membrane which may be granulated or knotty in parts, owing to cell infiltration and to hyperplasia. There are torulose folds in the mucosa or even polyps, which may be attributed to unsuccessful efforts at healing on the part of the mucosa. Varying amounts of mucus and mucopurulent pus may be seen, in some cases as curtains or coatings, in others, welling forth in great quantities.

Generally no ulcers are seen in the early stages of *colitis gravis*. At later stages there are smaller or larger, often confluent ulcers mostly in the lower portion of the intestine. There are instances in which the rectum is free from ulcers, while

TABLE 1

Age and Sex Distribution

	Stage 1.		Stage 2.		Stage 3.	
	Women	Men	Women	Men	Women	Men
10 – 20	1			3		1
20 – 30	1	1	2	4		1
30 – 40		1	2	5		1
40 – 50	1	2	2	2	1	
50 – 60			1	1	1+	
60 – 70			1		1	1
Total	3	4	8	15	3	4

blood-stained pus and radiologic findings indicate the presence of ulcers. In these cases they are evidently situated higher up in the colon.

Proctoscopic examination may sometimes be rendered impossible by anal spasms. It should be mentioned here that the examination is not entirely without risk. Apart from purely technical errors—there is always the danger of perforating the rectum, unless the instrument is introduced and kept under constant control by the eye—the fragile, diseased mucous membrane may easily be injured and the condition thus exacerbated. Proctoscopy (after the case has been diagnosed) should therefore not be applied in control examinations more often than is absolutely necessary. In order to avoid injuries caused by the thermometer, the temperature should not be taken by rectum.

When the process extends above the rectum, radiography shows, in most cases, the characteristic tube-shaped picture of the colon without haustra, sometimes with jagged contours indicating ulceration. The radiograph gives a clear conception of the extent of the process but the radiologic appearance shows

astonishingly few changes in those cases where the processes have healed satisfactorily from a clinical point of view.

Differential diagnosis usually involves no difficulties. Cancer and some rare forms of colitis (eosinophile colitis, gonorrhea, lymphogranuloma inguinale) may readily be ruled out.

As already mentioned, the stools may assume different consistence. When the disease is most severe, they have the consistence of gruel or water with large quantities of mucus and blood. Putrefaction of the feces is the rule but fermentation also occurs. Increasing firmness of the stools is a sign of progressive improvement and the final result, normal daily evacuation, indicates that the treatment has been successful. When this stage is reached, obstipation is likely to set in. The healing process is then jeopardized by the irritation caused by the hard lumps to the mucous membrane which will remain sensitive for a long time. On the other hand, there are many cases in which the mucous membrane shows good healing while the stools remain fairly frequent and loose although there is no tenesmus. The impression is that the muscular mechanism of the intestine has sustained an irreparable injury and retains the bad habit of expressing abortive feces.

The commonest complications, hemorrhages, anemia and the formation of abscesses, have already been mentioned. More severe strictures as a result of the disease are unusual. Carcinoma cannot be ruled out. Svartz has recently reported several cases in which the disease had been of long standing and may even have been in the process of healing, when cancer was diagnosed. Articular symptoms in the form of mild polyarthritis appear in some cases. Sepsis may occur. Nephrosis is observed now and then, especially in children, although it may subside, if the disease in the intestine is cured.

Avitaminosis rarely appears in manifest forms. Perhaps the most common to be observed is pellagra. With the first sunshine in spring blackish brown pigmentation may appear on the upper lip and the dorsum of the hands, and disappear on treatment with nicotinic acid. Undoubtedly, other forms of avitaminosis occur in severer cases, particularly B, C and perhaps A avitaminosis. The objective evidence for this is fairly scant, although treatment with vitamins in many instances has shown conclusive results in the form of improvement in the general condition.

The disease shows a varying course. In some cases a severe ulcerative colitis develops in a few months. In others, the disease may for several decades show periods of exacerbation in connection with acute intestinal infections, constipation or common respiratory infection.

Prognosis depends above all on the immediate treatment of the patient. In this connection it should be strongly emphasized that all cases of *colitis gravis* should be treated in a medical department, and in the sequence, be controlled in this department, if possible, by the specialist who has treated them from the beginning. In severe cases the patient may recover completely. Thanks to chemo-

therapy we now have new means at our disposal, which will be illustrated below. In the fatal cases, which are now rare, sepsis usually occurs at the final stage.

Thus, the most important thing is to recognize the disease at an early stage. The physician who does not possess a proctoscope and is not accustomed to its use, should send to the hospital all cases of non-acute diarrhea which cannot at once be proved to be harmless, such as gastric diarrhea, fermentive colitis, and constipation diarrhea. The last-mentioned, in particular, is a dangerous diagnosis.

TABLE II

Cases Treated Successfully With Salazopyrin

Result	Stage 1.	Stage 2.	Stage 3.
No symptoms, no relapse	7	8	1
No symptoms, after one or several relapses		3	
Improvement, no severe relapse		1	
Improvement, after one or several relapses		3	

Treatment:—The importance of the diet has formerly been exaggerated. In this disease a strict diet is useless. A prolonged strict dietetic treatment must be regarded as a professional blunder which leads to further emaciation and reduced power of resistance in the patient. An easily digested mixed diet, i.e., ordinary light food with the exclusion of coarse, spicy, salty, fat and fried ingredients, is quite satisfactory. Individual modifications must always be taken into consideration. Sometimes an antifermentative diet must be prescribed, and in some instances the

TABLE III

Cases Treated Successfully With Salazotiazol and Sulfalyl*

Result	Stage 1.	Stage 2.	Stage 3.
No symptoms, no relapse		4	1*
No symptoms, with one or several relapses		1	
Improvement, no severe relapse			
Improvement, after one or several relapses		1*	1*

patient must be kept on a diet of apples for a few days if there is marked putrefaction. Other recent experiments to treat the disease by changing the intestinal flora, may be mentioned in this connection, e.g. by giving Procolon* which contains colibacilli, and which in some quarters is considered to have a favorable action. As mentioned previously, administration of vitamins is an important factor. Besides improving the general condition, Vitamins A, B, and C may be said to

*Manufactured in Sweden by Kronan.

have a certain effect on the power of resistance and the permeability of the mucous membrane. Parenteral administration must often be resorted to. In hypoproteinemia which may be present in the absence of complicating nephrosis, proteins or aminoacids must be given. The effects of the preparation Aminosol† given intravenously have been reported to be excellent. Blood transfusions may also be given. They are necessary if there has been heavy loss of blood when the patient is admitted. In less severe cases blood transfusions have a very favorable roborant effect.

As substitute treatment, ferrotherapy plays an important part in all cases of sideropenia with or without manifested anemia. In most cases ordinary iron preparations are sufficient, e.g. tablets of ferro-tartrate, but it may be necessary to resort to less irritating drugs.

In extreme cases of diarrhea, bismuth, tannalbin or opium must be given, and spasmolytics in the form of belladonna, papaverine or Skopyl*, which is a methylscopolamine nitrate and an excellent preparation, should be given for tenesmus.

The treatment of the disease process:—A few words will first be said about the surgical treatment. Resection of the colon has been tried earlier and has lately become popular in some quarters. I have had no experience with this method. The operation, which appears to be a fairly serious intervention, is in some cases followed by severe conditions resembling pernicious anemia, and should under no circumstances be applied in the first place.

Intestinal (cecal) fistulas, in order to drain the intestine and also to rinse it with suitable media, now play a very restricted part. In the severe cases where this operation is resorted to, the process does not seem to be checked, but to creep on irrespective of the intervention. During the seven years that I had the opportunity of studying Nanna Svartz' material of colitis at the Seraphimer Hospital and the Caroline Hospital in Stockholm, this operation was not recommended in any of the cases. Now and then, severe cases were seen in which cecostomy had been performed in other clinics, and in which the fistula could be closed in due time without ill-effects. The patient under favorable conditions, especially with chemotherapy, recovered completely.

In this country specific treatment, if I may use this expression for antibacterial internal therapy, was applied earlier fairly successfully by Nanna Svartz in the form of treatment with enterococcal vaccine and serum. After chemotherapy had been introduced by her and Kallner, it was also applied in her clinic in isolated cases.

The first real progress was noted with the use of sulfapyridine. In many of the severe and long-standing cases the diarrhea decreased after a few days, the mucous membrane became pale and healed. After Svartz had tried Salazopyrin (salicylazosulfapyridine, Pharmacia) originally intended for polyarthritis, in this

†Manufactured in Sweden by Vitrum.
*Manufactured in Sweden by Pharmacia.

disease, she found that it produced a still better result, and at the present time the treatment is advantageously started with this preparation, usually in doses of two tablets, five to six times a day. Should this prove unsuccessful, Salazotiazol (salicylazosulfathiazole, Pharmacia), also introduced by Svartz, may in some cases give a good result. In some quarters Sulftalyl (phtalylsulfanilamidothiazole, Pharmacia) is also tried. This preparation is among the best, whereas in my opinion sulfaguanidine is valueless. As it is generally impossible to know beforehand whether a case will react favorably or not, we can only try the different preparations, and on trying one, we must not change it until it has been found to be ineffective during a considerable period. The side-effects of the preparations will not be discussed here. It should be mentioned that Salazopyrin and Salazo-

TABLE IV

Others (No Obvious Effect of Any Sulfa Preparation)

Result	Stage 1.	Stage 2.	Stage 3.
No symptoms, no relapse			
No symptoms, after one or several relapses		1	
Improvement, no severe relapse			
Improvement, after one or several relapses			
No improvement, one period of treatment			
No improvement, several periods of treatment		1	2 + 1 (previous effect with Salazopyrin)
Deterioration			
Died			1 (perforative peritonitis after 6 weeks treatment)

tiazol often cause exanthema, occasionally renal lesions with symptoms of lithiasis, and only in very rare cases agranulocytosis. In some cases the colitis may be exacerbated. The diarrhea may occasionally change into constipation, in which case paraffin must be given.

The common feature of all these sulfa drugs is that they are absorbed much slower and eliminated through the intestine to a greater extent than sulfapyridine, sulfathiazole and sulfamerazine. It should perhaps be mentioned that Salazopyrin may be useful in mild forms of colitis, such as fermentive colitis. The effect is undoubtedly due to the action of the preparation on the intestinal flora, although feces do not become sterile. The treatment requires a long period of time with a wide margin. The period of adjustment after the patient has been discharged from the hospital, and the early period on his return to work, are particularly important.

Penicillin is effective only in cases where sepsis of penicillin-sensitive bacteria occurs. Theoretically streptomycin should be effective. Successful preoperative treatment is reported from America, particularly in cases of cancer of the colon, with sterile feces as the result. In Sweden some cases have also been treated successfully with streptomycin. I have tried the treatment in only one case, with large doses for one week. During this period the patient's condition deteriorated markedly. Moreover, as streptomycin is highly toxic, and in many cases causes severe injury to the eighth cranial nerve with consequent permanent deafness, I have no faith in streptomycin in its present form as a therapeutic agent in this disease.

Local treatment with different chemical preparations is often effective, at least after the ulcers have begun to heal and the formation of pus has lessened. Enemas with ⅛ to ¼ per cent collargol (colloidal-silver), 2-400 ml. every second day, to be retained for 20 minutes, are in many cases, extremely effective. The treatment may be continued for at least a month without the risk of argyria. Dermatol powder, as well as sulfa preparations in the form of powder, suppositories or enemas, may be useful in some cases. Tannic acid enemas belong probably to a past phase.

Finally, a short survey will be given of material from Falu hospital from 1944 to the autumn of 1947, inclusive. The material comprises 37 cases of ulcerative colitis.

For the sake of lucidity I have divided the material according to three supposed stages, namely:

Stage 1:—Slight but typical changes in the mucous membrane of the rectum, but without ulceration or radiologic changes.

Stage 2:—More severe changes in the mucous membrane, hemorrhages of the mucous membrane and as a rule visible ulcers and tubular shape of a larger or smaller portion of the colon.

Stage 3:—The most severe cases with fever or sharp rises in temperature, increased sedimentation rate, anemia and emaciation.

This rough division must, naturally, be very schematic.

Table I shows the age and sex distribution. There are more men than women in the material (23 to 14). Stage 2 dominates. Notable is the number of 9 men and 4 women 20-40 years old.

Table II is a record of 23 cases treated successfully with Salazopyrin, that is, cases in which the condition improved, the symptoms disappeared and the stools were of normal consistency and frequency within a week or two. As seen from the table all cases under "Stage 1" have recovered, 11 "Stage 2", and one under "Stage 3".

Table III is a combined record of the eight cases treated with Salazotiazol and Sulftalyl. These preparations have been tried in cases where Salazopyrin had no obvious effect. Also in this group, one "Stage 3" has recovered, and one has improved.

Table IV shows the six cases in which no improvement occurred on treatment with the above-mentioned sulfa preparations. One patient recovered after the preparation was discontinued. One patient died from perforative peritonitis.

Thus, notwithstanding the relatively short observation time, the records show the good results that may be obtained from treatment with Salazopyrin and similar preparations, particularly at an early stage of *colitis gravis*. Including the advanced cases, however, 21 out of the total number of 37, recovered and had a daily, normal evacuation after only one stay in the hospital, and 4 others recovered after several periods of treatment. This shows, once again, the importance of hospital treatment at the earliest possible stage.

SUMMARY.

A brief description of *colitis gravis* is given, and the importance of early diagnosis by means of the proctoscope is emphasized. The most important therapeutic progress is the introduction of chemotherapy in the form of Salazopyrin, (Svartz) and similar preparations. This is illustrated by the author's own material of 37 cases from a Swedish central hospital.

N.B. This paper was written before the author became aware of the investigations on lysozyme in stool specimens as they appear in Grace, Seton, Wolf & Wolff: Am. J. M. Sc. **217**:241, 1949.

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CORTICODIENCEPHALIC GASTROINTESTINAL SYNDROMES IN EPILEPTICS*

(Part VIII)

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Material and Method

In order to choose the proper material from a collection of 5,000 admissions to the institution for epileptics so that such material could fit into the symptomatology of the corticothalamomammillary tract or the final common pathway as neurogenic gastrointestinal cases is far from an easy task. The burden of proof as to whether the particular lesions are near the ventricular system or are purely cortical, lies at our doorstep. The decision as to whether the patients suffer from a lesion that interferes with the former or latter pathways, must be arrived at not only on the mere presence of localizing aurae but also on the supplemented neurological findings. Even encephalographic findings to back up the above, will not produce a complete picture. Every possible relevant fact dealing with each case record must form part of the analysis of the data to be presented, because the literature, even on the clinical data of water metabolism alone, offers almost every conceivable type of neuropathologic lesion from neoplastic, to traumatic, to degenerative. In their analysis of the gastrointestinal material in relation to epilepsy up to the year 1929, Lennox and Cobb considered the entire field of gastroenterology in conjunction with this disease. They were not concerned with special syndromes. However, in their data of the clinical material dealing with the gastrointestinal tract of epilepsy, there were evidences of motor and secretory disturbances of the gastrointestinal tract which could be placed on a neurogenic control basis, either into the corticothalamomammillary tract or the other. Furthermore, they did not present any clinical work which would favor the final common pathway because of the association of positive neurological findings together with the gastrointestinal motor and secretory symptoms since presumably the epilepsy was of the so-called idiopathic type.

In his analysis of the literature, Sheehan, like Lennox and Cobb, also followed the scheme of motor and secretory disturbances of the gastrointestinal neurogenic control mechanism. His data, too, could be fitted into the corticothalamomammillary or the final common pathway. Here again, as in the case of Lennox and Cobb, no material was presented to indicate that the final common pathway might, on a

*Read in part before the Thirteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 7, 8, 9, 10 June 1948.
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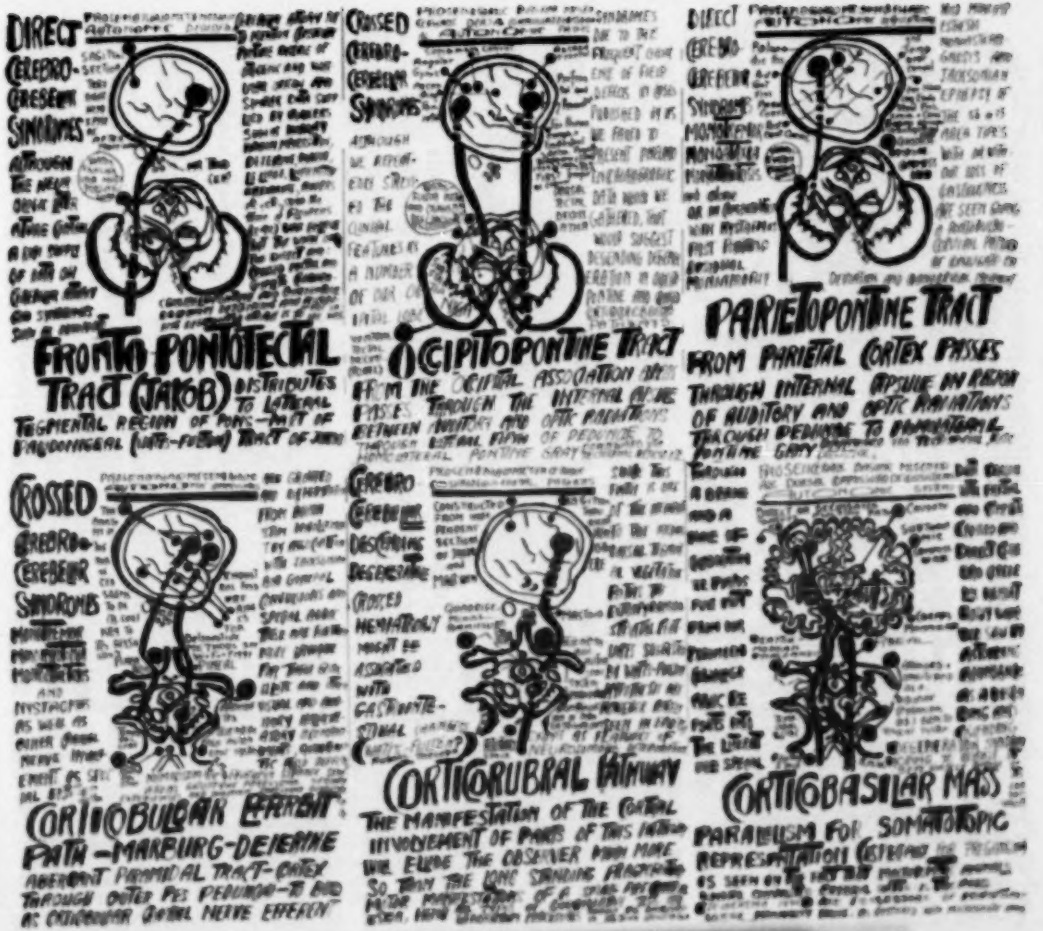

Fig. 56—Top left, Fig. 57—Top center, Fig. 58—Top right, Fig. 59—Bottom left, Fig. 60—Bottom center, Fig. 61—Bottom right.

sympathetic or parasympathetic basis, be the tract that controls neurogenic function of the gastrointestinal system. In the literature which was presented by Hare, however, there is an abundance of material of the infectious, traumatic, neoplastic and other pathological data associated with neurological findings in some cases, so that the neurogenic control of water metabolism could be placed either in the corticothalamomammillary or the spinothalamic pyramidal system routes. Rosett's data on the cingulate system could also fall along the line of subserving to motor and secretory phenomena of the gastrointestinal tract. The cingulate system subserves the autonomic in general with no special predilection for the gastrointestinal system except according to some authors. Although we repeatedly expressed our views in favor of the cingulate system as being a neurogenic gastrointestinal cortical representative we are at times led to believe that the areas in the frontal region as favored by Watts and Fulton are more important in this connection. Whether the preoptic system, or the mammillothalamic pathway to the cingulate, or both, control gastrointestinal function, the future will decide. The data by Watts and Fulton and Watts and Frazier could, however, be, because of its emphasis upon cortical stimulation, placed, either into the corticothalamomammillary system or into the final common pathway, since both of these systems, due to the fibre tract being of a centrifugal or centripetal type, could be construed to begin or end, within the cells of the cerebral cortex, which, in the frontal and other regions are the starting or finishing points in the frontal of the corticothalamomammillary as well as the final common pathway system. We simplified the anatomy of the corticodiencephalic and diencephalocortical pathways and their connections throughout the cerebrum, by giving the structures centered at the base of the cerebrum the designation of the body of a basket from which a handle radiates into the lobes of the hemisphere. The description of the handle was simple enough. A great deal of indecision was encountered with the geometric designation of the floor of the diencephalon. On some occasions we used the term polygon, and on others the word polyhedron was employed. From the radiating tracts that enter and leave this space it becomes evident that we are dealing with a dysmorphous structure which forms the body of the basket.

Our material, therefore, in regard to its relation to either the corticothalamomammillary or the final common pathway symptomatology, can be said to resemble the collection of data by Hare and to a certain extent that of Watts and Fulton and Watts and Frazier. Unfortunately, however, Hare's material dealt only with one feature, namely water metabolism excluding the problem of gastrointestinal and that of the convulsive mechanism. The material of the other three authors, however, dealt both with the gastrointestinal and urinary system thus being related questionably to water metabolism also. Watts and Fulton and Watts and Frazier, however, did not deal with the problem of convulsions. Furthermore, their data in almost all of their work on this problem, was confined mostly to experimental rather than clinical material except for an isolated paper by Watts or a number of citations from the literature that presented clinical cases.

Fig. 62—Top left. Fig. 63—Top center, Fig. 64—Top right, Fig. 65—Bottom right, Fig. 66—Bottom center, Fig. 67—Bottom left.

Before we are to attempt the presentation of actual cases or syndromes which fall into the cortical diencephalic neurogenic control of the gastrointestinal and urinary function we have three major problems to face. The first problem is that of the nature of and extent to which gastrointestinal disturbances of any kind are associated with epilepsy and its incidence in 5,000 consecutive admissions to an institution for epileptics, covering a period of over 50 years. The second problem which we face, is the selection of cases with gastrointestinal and urinary aurae from the above number of patients so that they could fit into definite syndromes. Each syndrome group would then have to be described not only in relation to the type of aura but also to the actual cause of epilepsy, to the type of seizures, to the time of occurrence of the same, to the neurological and pneumoencephalographic data, etc. The third major problem is that of causation and cerebral localization of the lesions of epilepsy in general and that of the gastrointestinal group in particular, the latter including the syndrome and nonsyndrome type of gastrointestinal cases.

Before we can proceed with the above three problems it will be evident to the reader that it is necessary for us to show how a detailed history, involving that of the history of epilepsy, the past personal history, the family history, etc., should be taken. The proper inquiry not only from the patient but also from the family directly, and even from distant relatives are all essential features in the obtaining of the facts necessary to the segregation of our cases. Because abdominal pain due to gastric, hepatic, intestinal, renal and ovarian disease is so common in medicine and surgery, we felt that a detailed history involving aurae that deal with this symptom is indispensable. We do not claim that a large number of appendectomies, cholecystectomies and ovariectomies were unnecessarily performed upon epileptics because of their paroxysmal and interparoxysmal episodes of abdominal pain. We know, however, that the average diagnostician would be prone not to stress this symptom complex or include it among the frequent items to be differentiated when his palpating hand leads him to decide between existence of an appendicitis as against a pyelitis, duodenal ulcer or gallstones in such individuals.

In addition to the obtaining of a history from the patient or the family, it was very often necessary for completing the records, to collect data from the various institutions, private hospitals, various neurologists and other medical sources. Although Muskens was adamant in his assertion that the taking of a history of the epileptic or his family involves a special technic we are not quite in agreement with him. For years we felt that many cases of institutional epilepsy consist of problems of general neurology, general medicine and neurosurgery. In the case histories we would note data on mastoiditis, mastoid operations and their arrested postoperative cranial symptomatology, such as mild petrositis, meningoencephalitis and otogenic self-limited hydrocephalus. In the above fashion we often felt that the skeleton in the closet of institutional epilepsy contains the residuals of secondary meningitis and encephalitis involving childhood diseases and covering the entire armamentarium of pediatrics and general medicine. These

arrested sequelae could not always exclude a ventriculitis of the third ventricle with its implication of the diencephalon. Although we feel that the family should be questioned much more in this epilepsy condition than in most other neurological conditions because the convulsive syndrome might be brought about by a variety of causes and produced by innumerable pathological conditions, yet we feel that all the other sources from which we were able to obtain our data were also of indispensable value, not only in the segregation of the gastrointestinal type of cases, but in particular with the division of our epileptic cases into certain etiological categories.

Since the material under consideration is taken from a collection of consecutive admissions over a period of 50 years, it will be evident to the reader that the advancement in medicine during this half a century plays a tremendous role not only because the views of the causation of epilepsy from that of heredity, diet, and so forth, to that of the strides made with chronic increased intracranial pressure caused by the collection of cerebrospinal fluid in the brain coverings with the subsequent dehydration theory as presented by Temple Fay. It should furthermore be remembered, that the data which was obtained during this 50-year period also varied with the progress not only in epilepsy but also in general medicine. Roentgenology was in its infancy during the first decade of the collection of our material. X-rays of the skull were therefore not advanced insofar as the presentation of such roentgenographic detailed evidences of increased intracranial pressure findings upon admission to the institution was concerned. Encephalitis particularly of the lethargic type, and other forms as well as infections in general and particularly the meningidities of the various forms, were not as definitely segregated during the first, second, and even third decade as they are today. Syphilis and tuberculosis progress had not reached their well-established extent of involvement of the brain and its covering at the time of the inception of the institution as they have today.

A problem as simple as heredity in epilepsy, is indeed complicated when one has to consider the fact that heredity in its broader sense, must be distinguished from the congenital and familial types of brain involvement. We have shown in previous publications that syphilis and other diseases produce congenital involvement of the brain and its coverings and thus cause epileptic attacks in an individual even after the second decade of his life, although in most instances during the first decade, and only mild neurological evidence of organic disease of the brain and its coverings caused by this disease were present at birth. Similar conditions could be mentioned. In this sense, therefore, there is such a condition as congenital epilepsy which is to be distinguished from that which is incidental to hereditary diseases. As everyone knows there are certain hereditary diseases which have a sex-linked character. Encephalitis of the macular type, and other conditions of the central nervous system are definitely hereditary although they may not be sex-linked. We could mentioned a number of such diseases, namely, Tay-Sachs disease, Schilder's disease, progressive muscular atrophy and so forth

in which epilepsy is not unlikely to occur. Heredity is rare in symptomatic but common in idiopathic epilepsy.

The taking of a detailed hereditary history covering a number of generations is therefore a very important item, not only from the standpoint of uncovering the incidence of syphilis and other related conditions, but also from the viewpoint of following the maternal and paternal branches of each family so that a true hereditary condition which is strictly so could be found operating in a causative way and thereby eliminating the term idiopathic epilepsy.

Another very important item is that of the investigation of trauma as a causative agent in the production of epileptic fits. The institution from which our material was taken being the largest in the state for individuals suffering from this disorder, derives its patients from various rural and suburban sections. Although such factors as automobile accidents are common to both localities and may predominate in one there are other traumatic causative factors which are almost restricted to one locality excluding the other. Trains, trolley lines, cellars, tall buildings and other objects may be the items which produce head injuries more frequently in one locality than in another and would therefore be elicited in the history, it being necessary that proper inquiry be made and that the patient and relatives be questioned regarding contact with such potential causative agents.

Before embarking upon the analysis of about 300 cases to illustrate the method of taking a history and for the purpose of comparing the aurae and other findings in ordinary 300 admissions with the syndrome gastrointestinal cases we will present the reader with the aurae of the gastrointestinal syndrome patients. Before each aura the substitute of the registration number will be shown so that the reader might gauge the relative time of admission. Thus registration numbers 1 to 99 extend over a period of 16 years beginning with the year 1898. The second thousand (numbers 100 to 144) registrations extend over a period of 7½ years from December 1915 until June 1923. The third thousand consecutive registrations (as represented by numbers 145 to 181) also extend over a period of 7½ years from June 1923 to December 1929. The fourth thousand consecutive registrations (as represented by numbers 182 to 240) extend over a period of 5½ years from December 1929 until April 1934. The fifth thousand consecutive registrations (as represented by gastrointestinal cases of 241 to 318 inclusive) cover a period of 6 years starting with April 1934 and terminating in May of 1940 with the number five thousand.

The exact number of cases showing gastrointestinal aurae is 326. In our direct experience as a result of personal questioning the incidence of these is more than four times this number at least. We thought it best, however, to follow the admission record since here the gastrointestinal symptoms constantly impressed the family and invariably drew the attention of the family physician. These cases, as the reader knows, have been chosen from 5,000 admissions. The eight missing cases will be added later. As we view the various aurae of our 5,000 cases we have an almost unrestrainable urge to mention autonomic aurae which by far exceed the number of gastrointestinal aurae and cover respiratory, cardiovascular and

involve all systems of the body. Due to the lack of space we shall desist from enumerating them. Following are the gastrointestinal aurae followed by the substitute admission number for the reader to refer to. Since the records of most institution material are privileged and confidential we are obliged to make substitutions of consecutive numbers for the actual registration number in presenting gastrointestinal aurae.

Gastric: 1, 17, 18, 20, 23, 24, 26, 27, 30, 31, 32, 34, 36, 38, 39, 40, 41, 43, 44, 45, 46, 47, 48, 49, 51, 52, 53, 54, 56, 59, 64, 66, 81 (readmission?), 86, 89, 92, 96, 102, 107, 109, 111, 114, 121, 131, 133, 134, 135, 136, 139, 140, 141, 142, 143, 153, 154, 159, 165, 167, 169, 170, 233, 252, 258.

Pain in stomach: 2, 5, 8, 12, 71, 72, 75, 76, 99, 103, 116 (readmission-69A), 118, 122, 128 (readmission-115A), 144, 145, 146, 147, 152, 160, 173, 176, 178 (readmission-158A), 179 (readmission-148A), 198, 210, 212, 213, 216, 218, 247, 249, 255 (readmission-235A), 224, 275, 276, 277, 287, 289, 304, 305, 310, 312.

Sensations, chest to throat: 3.

Throat irritations, groaning, shaking of hands and feet: 4.

Pains in abdomen: 14, 127 (readmission-112A), 200, 206, 215, 237, 266, 278, 296.

Burning stomach: 6.

Distress in stomach, rises to ears and head: 7.

Choking sensations: 9, 91, 98, 112, 174, 181, 217, 222, 226, 293.

Lump rises from stomach to head: 10.

Vomiting: 11.

Begins in epigastrium: 13.

Sees and smells something and stomach?: 15.

Epigastric pain: 16, 60.

Twitching of the mouth and sucking: 19.

Nausea and gasping: 21.

Mouth feels drawn: 22.

Epigastric distress: 25.

Epigastric flushes: 28.

Gastric and cephalic: 29.

Gastric and cry: 33, 35.

Desire to urinate: 37.

Gastric and psychotic: 42.

Blindness and choking: 50.

Nausea and vertigo: 55.

Epigastric and dizziness: 57.

Epigastric: 58, 61, 62, 123, 300.

Gripping sensations in stomach which rise to head accompanied by dizziness: 63.

Feeling lump in stomach: 65.

Peculiar feeling in the abdomen: 67.

Gastric sensation: 68.

Feeling in the stomach: 69, 101, 149, 150, 151, 164, 171, 180, 188, 195, 199, 209, 227, 229, 234, 240, 241, 256, 268, 269, 280, 286, 308, 311.

Pain in the stomach and heart: 70.

Hungry feeling: 73.

Nausea and numbness in hands and fingers: 74.

Choking and feeling of pin and needle sensation in right hand: 77, 78 (readmission—equals same symptoms).

Distention of stomach: 79.

Sour taste in mouth: 80.

Peculiar feeling in mouth: 83.

Pain in neck: 84.

Sick in the stomach: 85, 161, 244.

Pain in stomach and choking: 87.

Gastric and peculiar feeling in stomach: 88.

Gastric and feeling of impending danger: 90.

Crawling feeling in stomach: 93.

Sick feeling in stomach: 94, 191, 250, 253, 257.

Funny feeling in stomach: 95.

Grinding of teeth: 97, 194.

Gastrointestinal pain: 100.

Sensations in the stomach: 104.

Numbness and weakness in the epigastrium: 105.

Dullness, stupidity and nausea: 106.

Solar plexus: 110 (readmission-98A).

Nausea and mental depression: 113.

Epigastric and nervousness: 115.

Gastric and sensory: 117 (readmission-57A), 175.

Nausea: 119, 125, 126, 182, 183, 186, 187, 192, 205, 207, 219.

Feels something creeping up from the stomach: 121.

Hungry feeling in the stomach: 129.

Gustatory: 130.

Nervous sensation about the lips: 132.

Pain in the left side of the stomach: 137.

Twitching in the mouth: 138.

Gastric disturbances: 148.

Queer feeling in the stomach: 155.

Gastric and constipation: 156.

Distress in the stomach: 157, 272.

Epigastric weakness: 158.

Abdominal: 162.

Gastric and visual: 163.

Thirst: 166.

Stomach: 168.

Vomiting or gagging: 172.
Chewing of mouth: 177.
Smells foul odor?: 184.
Stomach feels funny: 185.
Sweats and drinks: 189.
Nausea and abdominal discomfort: 190.
Something rises in stomach: 193.
Rising feeling in stomach: 194.
Choking in the throat: 196.
Grinding of the teeth and yelling: 197.
Thumping in the stomach: 201.
Asking for water and paralysis partial of the left arm: 202.
Peculiar sensation in the stomach: 203, 228, 281.
Drawing sensation in the abdomen: 204.
Nervousness and pain in stomach on the day before: 208.
Feeling in stomach and dizziness: 211.
Strange feeling in the stomach: 214.
Peculiar feeling in the throat: 220, 230, 232.
Peculiar sensation in the abdomen?: 221.
Sick feeling in epigastrium and dizziness: 225.
Peculiar feeling in the epigastrium: 231, 235, 309, 314.
Sensations in abdomen: 236, 302.
Distress in stomach: 238.
Stomachache?: 239.
Excess of gas for days before the attack: 242.
Sick stomach: 243.
Sickness in jaw at times: 245.
Twitching in the mouth: 246.
Weak feeling in left side: 248.
Weak feeling in stomach: 251.
Drawing of the mouth and numbness: 254.
Rolling in stomach at times: 259.
Dumbness and lump in abdomen: 260.
Asks for water: 261, 317.
Vomiting and nausea: 262.
Sounds and odors become strong: 263.
Drawing sensation in the stomach: 264.
Feels a lump in the stomach: 265.
Pressure in epigastrium: 267.
Pain in stomach and muscles of stomach contract; also pain in chest: 270.
Numbness in abdomen: 271.
Gastric sensations: 273.
Something comes up from the stomach into the throat: 274.
Sickness at stomach and imaginary noises: 279.

Blood rushing from the epigastrium to the head: 282.
Sensation in the throat: 283.
Cramps in left side?: 284.
Gurgle in the throat: 285.
Abdominal discomfort: 288.
Feels as though his bowels are going to move: 290.
Peculiar feeling in the right side: 291.
Bloating of the stomach: 292.
Occasional rattling in the stomach: 294.
Tightening and jumping over nerves through the stomach and chest: 295.
Sick to stomach and dizzy: 297.
Dry feeling in the mouth and dizziness and shaking all over: 298.
Lump in throat and queer feeling in back of head: 299.
Stomach hurts: 301.
Feeling from head to stomach: 303.
Choking sensation in epigastrium: 306.
Nervous feeling in stomach and eyes draw to one side: 307.
Something in stomach: 313.
Sick feeling in epigastrium: 315.
Occasional choking sensation: 316.
Feeling in the stomach, tightening of left hand and tightening above the elbow: 318.

In the above the reader has seen a variety of aurae which essentially referred to gastrointestinal and urinary systems some of which indicate an upset in water metabolism manifested by the sensation of thirst, or other similar manifestations.

Eventually we will segregate the above types of aurae into various syndromes as we have stated before. It may be seen on the basis of the aurea alone, one can decide as to whether the march of events constituting an epileptic attack took place in the mammillothalamic pathways or that it was impossible because of the occurrence of visual, auditory or other sensations, or some special type of paralysis that was associated with the gastrointestinal aurae thus necessitating it to have transpired only because of impulses that travel through the cerebral cortex and downward by the way of the final common pathway. In order for such aurae to be classified either in the corticothalamomammillary or the other pathway it is of course essential that additional data noticed within the neurological findings, pneumoencephalographic, as well as complete historical material that might point to the nature or extent of the lesion, be included. For this purpose we have assembled the incidence of certain aurae, the occurrence of various types of brain injuries or brain diseases, the incidence of various types of attacks, the extent of occurrence of nerve injuries and developmental disturbances, and finally the incidence of nervous diseases, including epilepsy on the paternal and maternal sides of the families in 300 cases of epilepsy. The 300 cases were not otherwise chosen for any particular purpose. These cases might well serve as a cross section of the incidence of data which was just mentioned in any number of cases taken at ran-

dom for gastrointestinal, autonomic, psychologic, or other investigations from out of the 5,000 consecutive registrations in the New Jersey State Village for Epileptics. These cases will show the reader how much data is obtained upon the admission of the average epileptic to an institution. It might furthermore serve as an indicator of the nature and extent of the data along the clinical neurologic lines mentioned in cases of gastrointestinal disturbances which we will later present and which do fall into definite syndrome groups. Finally, whenever possible, in the presentation of data within the syndrome groups which we intend to eventually segregate from the aurae presented above, the reader might find it interesting to refer to this historical analysis of the 300 cases which we are about to offer. In the 300 cases which consisted of all types of epilepsy irrespective of the incidence and aurae there were noted about 35 aurae. This would make the aurae incidence roughly about 10 per cent which is far below that observed in the average. In the following, aurae as well as prodromata are all considered under the heading of the former. In only 3 cases typical prodromes really occurred. These aurae can be divided roughly into sensory, psychic, motor, and, although some of them can be classed into autonomic we chose to confine ourselves only to the former categories. The following sensory aurae consisted of: general sensations, sometimes dizziness and seeing things, jumping feeling on the inside, numb feeling, sick feeling, nausea, nervous feeling, pleasant sensation throughout the body, lump in the throat, feeling in the head, vertigo, choking sensations and shortness of breath, tightening and jumping nervous feeling in the stomach and chest, queer feeling in the eyes, feeling tired before attacks, dizziness before attacks, chills before seizures, numbness of fingers, faintness, headache, lump in the stomach and throat, rattle in the stomach and finally stiffening sensation in paralyzed leg. Under the heading of psychic aurae there was merely the term psychic, or part of a sensory aura such as seeing things, or shakiness and weak feeling with hearing of imaginary noises and seeing of imaginary objects, or being violent before and after attack, fright, delusions, and hallucinations, etc. The motor aurae were the least frequent. In one, just the word motor, was used. In another, there was a twitching of the right eye several days before attack, in another there was diplopia, and in a fourth, the calling for help might be classed under motor. It is important to stress that even seemingly insignificant items such as diplopia, when connected with gastrointestinal aurae are of tremendous importance. This might be localized in many places in the cerebral cortex not necessarily in the frontal region. It merely indicates disturbed extraocular muscle action. It may also result from lesions in the diencephalon. In our references to the work of Davison and Goodhart and to that of Muskens we encounter this phenomenon. Muskens in particular linked the 3rd, 4th and 6th cranial nerves which would be productive of diplopia in disease of the interstitialis region and nucleus of Darkschewitsch thus connecting parasympathetic centers and even sympathetic ones (Edinger-Westphal nucleus) with diplopia, showing how gastrointestinal neurogenic control operates in the midbrain. The above data in a few aurae above thirty, taken from the 300

cases is very little representative of a cross section of the type of aurae encountered in the 5,000 cases. This shows how our selected group of gastrointestinal cases, though presenting an aura in every patient might be deficient in other data. The aurae of these 300 cases although few, indicate however, that almost every portion of the cerebral cortex, whether its function is sensory or motor, may be associated with the epileptic attack in the way of disturbed function immediately before the attack,.or in the form of a prodrome which lasts for a few days before the actual occurrence of the seizure. Although some of these aurae might indicate that the sensory disturbance is located peripherally such as in definite pin and needle sensations or in the occurrence of vertigo or headache, it is nevertheless evident that the cerebral cortex is largely responsible for the march of such events. See Fig. 11 for specific localizations.

It has been pointed out before, that the causation of the epilepsy and therefore the possible clue to the existence of a lesion either in the cerebral cortex gastrointestinal localization of the frontal lobe or in the neighborhood of the mammillothalamic tract or within the area of representation of the pyramidal system is important. The incidence of such causes as given upon admission of 300 cases will orientate the reader as to the probable percentage of actual organic lesions in 5,000 cases and therefore reflect to some extent upon the causation which we will present only partially with our gastrointestinal syndrome cases. In our syndrome cases, however, the temporal relationship of aura to the onset of the seizure was completely worked up whenever given. The assigned cause upon admission, however, has not been thoroughly checked in some instances by direct interrogation for details that are not elicited in the ordinary medical history taking. The following assigned causes are therefore a cross section of the opinions of the relatives and the physicians in the cases. Among these are: cerebral hemorrhage, change of milk, fall on the head, constipation, loss of daughter, fall, fright, stomach, cerebrospinal meningitis, indigestion, teething, diphtheria, skull fracture, pregnancy, heredity(?), eating spoiled cheese, over-feeding, encephalitis after vaccination, gas on the stomach, concussion, shock during war and poisoned gases, intestinal disturbances, struck his head against a lamppost and was unconscious for 3 hours, asthma, kick in the abdomen, menstruation, using scabs to vaccinate in Germany, mother frightened two weeks before confinement, instrumental delivery, alcoholism, sorrow over sister's death, infantile paralysis, crushed foot, blow to front of head, temper, worms, run down condition, intestinal poisoning, appendectomy with drainage, pin worms found in appendix, mastoidectomy, dentition, shock at mother's death, burn and finally excitement when mother threatened to strike her. It is data such as the above that we found in most of the cases upon admission to the institution. With the type of cause as well as with some of the neurological findings which we will present later, it may be noted that, as the years advance nearer to the present, the assigned causes as well as the clinical neurological showed a more thorough and more scientific character. The development of the x-ray technic and the improvement in the laboratory method may be

given as the other factors responsible for the establishment of a more practical causal relationship in a larger number of cases than previously. The hereditary history, however, has been thorough all along, and of unusual value. This, however, was usually traced upon admission in practically every case and previous records, except when the patient was hospitalized at a neurological center or mental institution, were of little value since in most instances little interrogation of the family had been done prior to admission, or it was unrecorded even though a competent psychiatrist was on the case. We selected 300 cases for study of past histories, etc., and did not use our gastrointestinal cases collectively for such a purpose because certain specific features which we wanted to stress as etiological factors, particularly with regard to congenital and familial disease, were not available to us at that time. We feel, therefore, that in the eventual evolution of each gastrointestinal syndrome group for etiological data, the reader would do well to compare it with that specified in the 300 nongastrointestinal cases.

Some of the data on the 300 cases seems defective, nevertheless. This was due to the fact that upon admission, some of the records were incomplete, or, if an appreciable amount of data was offered, a large percentage of it was etiologically irrelevant. We have shown in our previous publication that such defects were remedied by the incessant work of the social service department of the New Jersey State Village for Epileptics which supplied the necessary additional material by working upon the record, by communicating with various institutions, and by even interrogating the families whenever necessary, even if it involved traveling long distances over the state of New Jersey. Some of this material, such as the age of onset of the epilepsy, we have repeatedly given in our previous publications. Thus in a study of 800 cases, (Weingrow, Fitch and Pigott 1941), we have shown that the average age of onset of the epilepsy was given as 11.2 years and the average duration of the epilepsy at 17.4 years. The above findings were present in the 800 institutional epileptics whose average age at the time of study was 28.6 years. Other items of interest were the type of seizure, the diurnal and nocturnal time of occurrence of seizure, and the seizure frequency. During a work of ten years with the aid of the prebellum social service department we have been able to remedy certain deficiencies of the records upon admission and fill the gap by our direct questioning of patients in the course of neurological examinations in an entire 5,000 cases caused by extramural lack of neurological investigation methods and other shortcomings. We have studied not only the seizure frequency and the type of seizures in the entire 5,000 cases but in a large percentage we have also noted the relationship of such items as grand mal, petit mal, Jacksonian and psychic spells in connection with a well established cause which is accepted in modern neurology, having a temporal relationship to the onset of the epilepsy. An example of this correlation is shown in one of our publications, (Weingrow, Fitch and Pigott 1941). In the above paper we have shown the relationship between the average number of seizures per year and the causation of the epilepsy. Following are the causes and the numerical data which represents the number of seizures

per year: alcoholism 10.1, meningoencephalitis 36.5, encephalitis 184.1, meningitis 51.8, syphilis 17.2, congenital syphilis 72.0, trauma 80.0, endocrinopathy 79.2, postoperative 70.0, infantile palsy 58.0, birth injury 154.0, congenital defect 48.0, pregnancy 50.5, tumor 22.2, familial disease 72.0, heat stroke 65.0, hypertensive encephalopathy 19.0, cerebral hemorrhage 101, congenital epilepsy 150.0, macrocephaly 139.0, congenital hemiplegia 102.0, unclassified hemiplegia 73.5, unclassified 91.5. In the above material, conditions such as endocrinopathy, pregnancy, tumor, familial disease, heat stroke, hypertensive encephalopathy, cerebral hemorrhage, congenital epilepsy, macrocephaly and congenital hemiplegia; all of these contain too few cases, namely three and below, for the seizure frequency as given, to be of any significance. The groups with the greatest number of cases were the unclassified series which contained 128 cases, trauma which contained 128 cases and birth injury and congenital defect which contained 48 cases. In a larger series than the foregoing we were able to study the incidence of aurae in 1,000 institutional epileptics. The figures on the incidence of present, absent and unrecorded, aurae in these cases will be summarized in the following paragraph. The importance of seizure frequency is self-evident. If extensive data dealing with it in relation to lesions in definite brain areas could be gathered, they might have some value from a prognostic standpoint. In the syndrome groups of gastrointestinal cases, the seizure frequency per year or per decade will be given whenever possible. This will indicate the frequency of associated gastrointestinal upset.

The reader will recall that in regard to the incidence of aura in the case history of 300 cases we remarked that some of the records were defective. We later showed that in some cases defects were remedied. In most instances clerical data was obtained by the various organizations in the institution as stated above. In the cases of seizure frequency as previously given and in the existence and type of aura, but especially in the former the nursing staff constructed records from direct observation. During the pre-war days and subsequently we studied these records and checked the report given from the various institutional sources as against those presented by the patient or relatives upon admission. In one of our publications (Fitch, Pigott and Weingrow 1939) the data on the incidence of aura is given in tabular form. This table shows that out of 1,000 institutional epileptics, aurae were present upon admission and otherwise in 295 cases, were absent in 482 cases, and were unknown in 213 individuals.

One can readily see how records on only 300 cases would be insufficient with which to compare incidence of aurae. Most sensory aurae, particularly if gastrointestinal sensory coloring is present, indicate action by the dorsal thalmus or modification by it of sensory impulses arising somewhere. An aura might therefore indicate pathologic involvement of the fibres that are connected with the centrifugal system advocated by Spiegel and others, as possibly connected with the olfactovisceral component of the dorsal thalamus and related to gastrointestinal sensory phenomena. In a future publication we intend to present the complete data of aura incidence in 5,000 cases. Upon analysis of that material we feel that

the average epileptic has an aura frequency which is greater than that which we presented in the 1,000 cases. Since aurae form such an important factor in the presentation of our material on the neurogenic control of gastrointestinal syndromes, we feel that the following additional data might be relevant and of special interest to the reader particularly since the relationship between them and the pathological lesions of the focal and general epilepsy depends upon this problem of aura. As we have repeatedly stressed in all our foregoing descriptions, such a relationship might give not only the extent of the lesion but also even its exact location so that we can decide whether an individual, with a characteristic aura belongs in that region within the cerebrum, governed by the corticothalamomammillomesencephalic system, or into the motor and sensory representation of the spinothalamic and pyramidal system category. In our 1,000 case analysis we found that out of 16 cases of alcoholism aura was present in 5; out of 29 cases of meningoencephalitis aura was present in 12, also in 11 cases of epilepsy due to encephalitis, aura was present in 3; in 19 cases of epilepsy caused by meningitis, aura was present in 3; in 11 cases of seizures caused by congenital syphilis aura was present in 4; in 18 cases of epilepsy due to syphilis, aura was present in 3; in 188 cases of traumatic epilepsy aura was present in 63 cases; in one case of trauma and endocrinopathy an aura was present; in five cases of seizures associated with endocrinopathy, aura was present in 2; in four cases where the onset of epilepsy was postoperative, aura was present in 3 cases; in 12 cases of fits associated with infantile palsy, aura was present in 8 cases; in 99 cases of epilepsy caused by birth injuries, aura was present in 28; in 110 cases of seizures caused by congenital defects, aura was present in 20 cases; in 6 cases of fits following pregnancy, aura was present in 3; in 4 cases of tumor aura was present in 3 cases. In conditions such as familial disease, electric shock, heat exhaustion, hypertensive encephalopathy, in toxic conditions and in sunstroke, the cases were too few for one to draw any conclusion whatsoever. In 11 cases of cerebral arteriosclerosis aura was present in 3, and in 447 cases consisting of unclassified epileptics aura was present in 128. Although the work of Penfield and many others indicates that a good percentage of most aurae, is due to irritation of the cerebral cortex, this does not exclude the diencephalon. Therefore, the mammillothalamic, the supraopticomammillary, the hypothalamic, the dorsal longitudinal fascicular system with its periventricular pathways and various other structures of the diencephalon, might produce the precursors of convulsions just as they would the convulsion proper. Every neurological finding is therefore important.

Now that the reader is familiar with the character, incidence and other probable details of aurae and seizures in 300 cases, their relationship to causation as given upon admission and otherwise, we will proceed with the latter subject and present additional data of assigned cause on admission in 300 cases. Items such as natural delivery, normal delivery, breech, instrumental, three weeks overdue, turning done, injuries about the head and neck, puny baby, delivered with arms over the head, cord wrapped around the neck, blue baby, forceps delivery, delivery

prolonged, injuries about the neck during delivery, difficult labor, cæsarian and premature birth, were all the items presented in the delivery record of 300 cases. Although the above presented no definite clue as to the possible location of a lesion in the brain which might have been caused by a birth injury, the reader can see that such admission records were valuable as follow-up material. With solid pathological material such as has been presented above, along lines of classification of neurological disease entities and causative factors in epilepsy, the reader will readily see that when the same is applied to the gastrointestinal group syndrome cases that actual focal lesions are present within the brains of these patients. We have in our previous publications invariably supported our etiological groupings with clinical neurological as well as pneumoencephalographic findings. An appreciable number of the gastrointestinal syndrome cases come from the material already published in tabular reference fashion.

Other items such as the age at which the patient began to walk was found in some of the case records. Some of the records were specific with regard to the various ages which, in instances such as walking at three years or two years, where data was contributory, and possibly also contributory, when the record merely stated "walked late". What has been said above with regard to the age onset of walking in the developmental history, was also true for the age at which the patient began to talk, and also the age at which the patient entered school. Although we do not intend, in the presentation of gastrointestinal syndrome groups, to delve extensively into material such as the above, we feel that such material is important even though we will, with the syndrome groups, only mention causation in specific cases. What has been said above with regard to the developmental history, may be repeated in relation to the progress the patient made in school. We must again impress upon the reader the need of our study of non-gastrointestinal cases. It might be the contention of reviewing epileptologists that the patient who presents a gastrointestinal aura is an individual who suffers from idiopathic nonfocal epilepsy. If such is the case then the past personal history is irrelevant as far as actual causes of the epilepsy is concerned. Moreover, the neurological findings might be incidental to the injuries sustained during fits. Our cases with gastrointestinal aurae were frequently associated with sensory and other focal aura, and hence most cases having aurae are Jacksonian. This being the case, the locale responsible for the seizure is also responsible for the gastrointestinal disturbance. The anatomy of such foci we have already elaborately covered in previous pages. We will refer to it by words such as mammillary body, etc., etc.

In the above data we were largely interested in presenting the reader with material which dealt with aura, seizures and causation as far as the relationship of the same to the admission record in 300 cases was concerned. Such data, exclusive of our investigations at the institution by directly questioning the patient and the examination of the same individual with regard to the exact cause and the possible aura, will be of unlimited benefit to other investigators who intend to

follow-up such problems, not only in institutional material, but also upon out patient clinical cases.

Throughout the presentation of the above data we reminded the reader here and there that not only the type of seizure, the aura, but also the cause are important. The importance of this as has been pointed out in relation to actual pathological findings within the cerebrum in our past publications cannot be emphasized sufficiently. In the first place such pathological findings are of utmost importance not only to the neurogenic control of the gastrointestinal and urinary systems but also the autonomic system in general. Before actually beginning with our syndrome material we even intend to present pneumoencephalographic findings or refer to them to show that the third ventricle is dilated in most cases upon which we performed this procedure. The relationship between pneumoencephalographic findings and the causation of epilepsy is self-evident. For this reason, although our original intention was to dwell upon gastrointestinal syndromes in particular and to mention other gastrointestinal findings in 5,000 cases, we considered that elaboration upon the cause of the epilepsy is very important not only from the gastrointestinal but also from the autonomic angle and its cerebral parts. This autonomic relationship the reader can very well see will explain the fact that during an ordinary convulsion, dilatation of the pupil and its contraction, and other evidences of autonomic activity are present. Some authorities even related the coma and somnolence after an attack to stimulation of the autonomic within the diencephalon and elsewhere.

Therefore, since we have dwelt to some extent on the causal relationship, we feel that anyone who plans to investigate the problem of epilepsy should not confine himself merely to the chief complaint of the individual as such, to the history of epilepsy, to the frequency of seizures, to the type of seizure, or to any other isolated fact which is mentioned by the patient or others in connection with the occurrence of the first fit. The investigator should dwell repeatedly upon the life history of the individual covering various abodes, various changes of addresses, various hospital visits that the patient has made in the past, even a long time before the epilepsy has set in. Conditions such as venereal diseases, childhood diseases and any possible neurological complications of the same, should be gone into in detail. Trauma is a very important subject, and has a definite relationship to various places where the individual has lived. Innocent and irrelevant appearing accidents, such as a fall from a baby carriage, from a bed, from a staircase, from a carousel, may be considered as mild incidents, but if carefully investigated in relation to the seemingly mild symptoms that followed for some time thereafter, are shown to be important factors in the production of convulsions. In all of our previous reports in the literature we stressed head trauma at birth or in childhood and their following train of symptoms as related to epilepsy. The newborn can't point to the traumatized caput and say, "Mother it hurts me here". Neither can the infant who hasn't learned to talk, complain of posttraumatic headache, or point to the fact that vomiting which followed a fall is associated with

headache and visual, sensory symptoms and mild or even moderate vertigo. The lack of explanation of symptoms caused by injury to the head in infancy and childhood must be substituted by other facts which should be elicited from every possible source, otherwise the diagnosis will be missed and the neurologist will be forced to use the term idiopathic.

The history taking of the epileptic is a domain in itself, as Muskens repeatedly stressed, and is exclusively by no means, the property of the neurologist. To substantiate what we have said above in regard to the taking of a detailed history, we offer the following 32 items which were chosen from the histories of the 300 cases which we are analyzing. Although some of these items might appear to be unrelated to the production of seizures in our investigation of the 5,000 cases, we have noticed that a good percentage of such data which was presumably given as unrelated to the epilepsy to have a definite temporal relationship to the onset of seizures. Some of the data such as infantile paralysis, sleeping sickness, chorea, cerebrospinal meningitis, encephalitis, slight stroke, nervous breakdown, meningitis, St. Vitus' dance, Schilder's disease, and even dropsy at six years, can be definitely conceived by the reader as having directly or indirectly affected the onset of the epilepsy. In regard to the pyramidal and extrapyramidal diseases mentioned above it is important to emphasize that it is at times difficult to differentiate between a pyramidal and extrapyramidal form of hemiplegia. For this reason Watts and Fulton, as well as Muskens, might still be right in connecting certain cortical areas with the former instead of with the latter. In many of our institutional hemiplegics we observed that the cerebral cortical changes were associated with a homolateral or contralateral ataxia and therefore with cerebellar descending degeneration. This does not put the case in the extrapyramidal system but indicates involvement of the corticopontine pathways. It is too bad that Muskens, who stressed cerebellar connections with cranial nerve action, did not fortify his experimental work with clinical proof often enough.

Other conditions such as measles, scarlet fever, swollen glands, pertussis, rickets, syphilis, diphtheria, gonorrhea, pulmonary tuberculosis, chickenpox, pneumonia, mumps, kidney condition, rachitis, tonsilitis, empyema, varicella, vaginitis at 7 years and chancre at 17 years, should all have a definite temporal relationship between the occurrence of the particular disease or condition and its possible neurological complications to the beginning of the epileptic attack. It should be impressed upon the investigator that not only we in our past publications, but Penfield and others, have repeatedly stressed the fact that any brain disease, whether it follows a disease of childhood or otherwise, could produce a certain definite pathological brain symptom local or general and that it would in some instances take not only one, two or three years, but even as long as between five and ten years for the onset of the first epileptic fit. No one, to our knowledge, has ever attempted a satisfactory reason for the delay of this phenomenon. We might be wrong, but it seems to one of us (Fitch) that someone somewhere mentioned that it takes time for the brain to produce circulatory changes or for the scars to

contract and in this way the cerebral circulation is eventually affected and the fit is produced. For many years we have pondered over this matter and could not come to a definite conclusion about it. Two of us (Weingrow and Pigott) have felt that progressive descending degenerative changes such as seen in cerebrocerebellar descending fibres or even ascending degeneration from the lower centers into and about the diencephalic areas might eventually produce ventricular, aqueductal and other dilatations and thus be related to seizures. Although the third of this collaborating team was the first to mention this mechanism he has thus far not whole heartedly been behind this idea even though he has seen definite air deficiencies in the encephalic pneumograms. The purpose of going into the detailed past personal history independent of the fact that others have not related diseases of the past to the onset of the epilepsy is very important. Most important, is the looking for neurological symptoms however insignificant, so long as they occurred in relationship to a severe systemic disease which was followed by brain symptoms.

(To be continued)

BOOK REVIEWS

STOMACH DISEASE AS DIAGNOSED BY GASTROSCOPY. Eddy D. Palmer, A.B., M.S., M.D., Major, Medical Corps, U. S. Army, Formerly Chief, Gastrointestinal Section, Walter Reed General Hospital, Washington, D. C.; foreword by R. W. Bliss, M.D., Major General, Medical Corps, The Surgeon General, United States Army. 200 pages, 53 black and white illustrations and 56 in color. Lea and Febiger, Philadelphia, Pa., 1949. Price $8.50.

In 1930, at Detroit, Michigan, the reviewer presented a new, semiflexible gastroscope with a focusing mirror and photographic camera, before the Section on Gastroenterology and Proctology of the American Medical Association.

Since then great advances have been made in the gastroscope and gastroscopy.

Dr. Palmer has written a very comprehensive and beautifully illustrated book with many case histories, which enhance the text.

Even physicians who do not do gastroscopy as well as those who do, will find this beautifully illustrated and clearly written volume a handy reference.

PUBLIC HEALTH IN THE WORLD TODAY. James Stevens Simmons, Brigadier General, U.S.A., Retired, Harvard School of Public Health; Assistant Editor, Irene M. Kinsey; foreword by James Bryant Conant, President of Harvard University. 332 pages. Harvard University Press, Cambridge, Mass., 1949. Price $5.00.

Very interesting reading is found in the first chapter of this volume. Here a description is given of an epidemic of smallpox and the vaccination of almost seven million New Yorkers. The use of smallpox vaccine dates back before the eighteenth century. In the colonies it was introduced in 1721, and not until Jenner announced the discovery that the virus of cow pox inoculation protects human beings against smallpox, did this method become popular.

It is recommended that the book be read carefully by the physician, social worker and others, who will find it interesting and educational.

THE 1949 YEAR BOOK OF PATHOLOGY AND CLINICAL PATHOLOGY. Howard T. Karsner, M.D., and Arthur H. Sanford, M.D. 543 pages, illustrated. Year Book Publishers, Chicago, Ill. 1949. Price $4.75.

This volume is divided into two parts, pathology and clinical pathology. A special article dealing with pathology of atomic bomb casualties on page 41, gives a comprehensive description of the aftermath of the atomic explosions at Hiroshima and Nagasaki. Hematologic and other studies in Hiroshima and control cities two years after the explosion, by Snell, Neel and Ishibashi are compared with results on 935 nonirradiated controls, and makes interesting reading.

The alimentary tract and associated glands are given full consideration. Fibrocystic disease of the pancreas, tuberculosis of the pancreas and viral versus toxic hepatitis, subchronic atrophy of the liver as compared with Laennec's cirrhosis, are fully discussed. Xanthomatous biliary cirrhosis; relation between serum lipoids and skin xanthomas with primary cirrhosis and electrophoretic patterns are some of the newer subjects found in this volume.

Shistosomiasis in gynecology, although not prevalent in this country, nonetheless is of interest because of the influx of people from countries where shistosomiasis is prevalent. In this abstract the reader will find a brief summary from the article in J. Obst. & Gynec., British Empire, June 1949.

Palliative testosterone treatment in women with advanced breast cancer after radical operations and postoperative x-ray therapy, showed optimal results with 25 mg. testosterone propionate daily for 8-10 weeks. In very advanced cases, especially those with advanced pleural, cerebral and liver involvement, hormonal therapy was ineffective.

On page 374 occult blood in feces using the benzidine test in patients who were receiving iron compounds, meat extracts, blood or were on meat free diets, showed that iron compounds failed to produce positive reactions. Meat extracts did not influence test results, while patients on meat free diet for three days gave negative benzidine reactions. This proves that a meat free diet is the only preparation required for the benzidine test. With benzidine less than 0.01 ml. blood results in a positive reaction. (The reviewer prefers guaiac as it is less sensitive).

Many other interesting diagnostic procedures are described which make this volume a desirable and necessary part of the physician's library.

An excellent author's and cross index completes the book.

THE PHARMACOLOGIC PRINCIPLES OF MEDICAL PRACTICE. John C. Krantz, Jr., Professor of Pharmacology, School of Medicine, University of Maryland, etc. and C. Jelleffe Carr, Associate Professor of Pharmacology, School of Medicine, University of Maryland, etc. 980 pages, illustrated. The Williams and Wilkins Company, Baltimore, Md., 1949. Price $10.00.

Here is a volume that the reviewer recommends to every physician and pharmacist. It not only describes the drug but it emphasizes its pharmacodynamic and pharmacotherapeutic action and its clinical application.

The value of this text is enhanced by the authoritative review and criticism by specialists in their various fields. For instance, penicillin is reviewed by Prof. Sir Alexander Fleming, streptomycin by Dr. Selman H. Waksman, etc. The tables and charts are valuable additions and the index is well prepared for ready reference.

The reviewer is impressed with the thorough and comprehensive description of the various drugs as one can readily see on page 445 where opium and its alkaloids are discussed.

Useful prescriptions complete the text.

ADVANCES IN INTERNAL MEDICINE, VOLUME III. Edited by William Dock, M.D., Long Island College of Medicine, and I. Snapper, M.D., The Mt. Sinai Hospital. Illustrated, 478 pages. Interscience Publishers, N. Y., 1949. Price $8.50.

The reviewer was fascinated by the array of talent contributing to this volume. Unfortunately the general practitioner neither has the time nor the inclination to read and digest the information found between the covers. It is somewhat beyond his scope and if I may be permitted to state, beyond his comprehension.

Only a limited number of our fraternity will be interested in purchasing the book and conscientiously reading it.

SYMPTOMS IN DIAGNOSIS. Jonathan C. Meakins, C.B.E., M.D., D.Sc., LL.D., formerly Professor of Medicine and Director of the Department of Medicine, McGill University. Illustrated, 542 pages. Williams and Wilkins Company, Baltimore, Md., 1948. Price $7.50.

In this edition the entire text has been revised and brought up to date. Several chapters were written by colleagues of Dr. Meakins and add to the value of the book.

The 10 Chapters into which the book is divided contain valuable information dealing with the entire human body. Three of the largest chapters describe the gastrointestinal system, the ocular symptoms and signs and the nervous system.

The text is clear, the illustrations are well done and the index is adequate. It is highly recommended.

FUNDAMENTALS OF INTERNAL MEDICINE. Wallace Mason Yater, M.D., Director Yater Clinic, Wahington, D. C. Third Edition. 1451 pages. Appleton-Century-Crofts, Inc., N. Y., 1949. Price $12.00.

Nineteen associates including Dr. Yater, have contributed to this outstanding volume on internal medicine. It is easy to read and easily understood. The medical student and the general practitioner will find it a ready storehouse of essential facts. Treatment is brought up to date as far as possible. In addition to diseases of the various organs, there are chapters on metabolism, allergy, intoxication, vitamin deficiencies, infectious diseases of the skin, ear, eye, and chemotherapy and therapy with antibiotics.

Various tables, differential diagnostic charts and a chapter on the physician himself complete the volume.

The illustrations are clear and the type and printing are excellent. At the end of each subject there are recommended texts for further reading. An extensive cross-index completes the book.

YEAR BOOK OF ENDOCRINOLOGY, METABOLISM AND NUTRITION. Edited by Willard G. Thompson, M.D. and Thomas D. Spies, M.D. 550 pages. Year Book Publishers, Inc., Chicago, Ill., 1949. Price $4.75.

Glancing over the table of contents, the reader finds that the editors have covered the field of endocrinology, metabolism and nutrition, and have selected for review the most instructive articles which the physician will find of value in his daily practice.

On page eight and the following pages there is a comprehensive review of adrenocorticotrophic hormone (ACTH). It seems that this particular hormone has all the virtues that physicians have been looking for during the ages. However it is a two-edged sword and the physician must learn its application and its contraindication in a given case. Further studies are required before it is finally accepted as the remedy par excellence.

On page 186 the reader will find Addison's disease which is fully presented from various angles. The testes, the ovaries, pancreas and liver are also reviewed. Page 391, the alimentary tract, page 407, the hematopoietic system, page 425, the cardiovascular system, page 446, the brain and nervous system, page 459, the genitourinary system, etc. receive careful consideration.

Malnutrition, therapy, and a good index complete the volume, which is highly recommended.

GASTROSCOPY: THE ENDOSCOPIC STUDY OF GASTRIC PATHOLOGY. Rudolf Schindler, M.D., F.A.C.P., Second edition. 433 pages. Ten full page colored plates, and many black and white. The University of Chicago Press, Chicago, Ill., 1950. Price $20.00.

This work is a revised edition (which first appeared in 1937) and is enlarged and much improved. This monograph, by a master of the subject, is indeed a classic of the highest order.

The gastroscopists, gastroenterologists, and clinicians will benefit by reading this book. This monograph will stimulate further interest in the value of gastroscopy as a definite and necessary aid in the routine studies required for the proper understanding of esophageal and gastric disease. Of course, gastroscopy does not yet fulfill all the necessary requirements for a complete study of *all of the stomach* but, with the combined work of the gastroscopist and the roentgenologist, one may now be able to avoid grave errors of omission and commission. This monograph is at the present the best work on the subject.

PROGRESS IN CLINICAL ENDOCRINOLOGY. Samuel Soskin, M.D., Director, Medical Research Institute, Michael Reese Hospital, Chicago: Dean, Michael Reese Hospital Postgraduate School; Professional Lecturer in Physiology, University of Chicago. 641 pages. Grune and Stratton, New York, 1950. Price $10.00.

This excellent volume on the progress and recent advances in Endocrinology by ninety-one experts, and under the supervision of Editor Doctor Soskin, an able metabolist and endocrinologist, should be, and is a welcome contribution to a recently acknowledged specialty in medicine! This book will be helpful to the student, practitioner, and specialist and to surgeon, clinician, and endocrinologist alike.

Among some of the contributors are: Astwood, Conn, Dolger, Glass, R. Levine, E. R. Loew, Lukens, Reifenstein, Ricketts, Rynearson, I. Snapper, Samuel Soskin, Strouse, Thorn, Van Dyke, Wilkins, Soffer, H. F. Klinefelter, and Zimmerman, Dolger, Soskin, Tolslot, and Martin who concisely and instructively present some of the problems in Diabetes.

J. W. Conn discusses spontaneous hypoglycemia. Kochakian discusses metabolic influence of the androgens.

Of interest is Ralli and Leslie's contribution on "The Role of the Posterior Pituitary in the Production of Ascites Associated with Cirrhosis of the Liver" (pages 557-762).

R. F. Escamilla presents "Simmond's Disease and Anorexia Nervosa (pages 525-535). S. J. Glass discusses "The Influence of the Liver on Sex Endocrine Functions", and briefly comments on human "Liver-Gonadal Syndromes". L. T. Samuels briefly considers the relation of nutrition to the anterior pituitary gland.

The role of hormones in metabolism by Soskin and R. Levine, and endocrine regulation of protein metabolism by Abraham White, of Los Angeles; the relationship of the endocrine glands to obesity by Soskin and Strouse, and the use of ACTH and (Kendall) Compound E in rheumatoid arthritis by the Michael Reese Research Group; and Wolfson's contribution on the role of hormones in the pathogenesis and treatment of gout (pages 595-604) are of considerable interest and bring the present-day accepted knowledge of these subjects to the reader, in an acceptable and understanding manner. The book is definitely one to be placed on every practicing physician's desk.

TEXTBOOK OF BACTERIOLOGY. Joseph M. Dougherty, A.B., M.A., Ph.D., Dean of the School of Science and Professor of Bacteriology, Villanova College, Fellow of the American Association for Advancement of Science, and Anthony J. Lamberti, B.S., M.S., Instructor in Bacteriology and Parasitology, Temple University School of Medicine, Formerly Instructor in Villanova College, member of the American Public Health Association. Second edition, 491 pages, 141 illustrations. C. V. Mosby Co., St. Louis, Mo., 1950. Price $5.75.

The "History of Bacteriology" (Chapter 1) in 17 pages is most interesting and informative. Other important chapters are those on the microscope and microscopy, culture media, bacterial types, effects of physical and chemical agents on bacteria; chemotherapeutic agents (19 pages) including neomycin, chloromycetin (chloramphenicol), polymyxin, aureomycin, streptomycin, bacillin, penicillin, gramicidin, etc. Also, briefly discussed by the authors are: infection, immunity, complement fixation, anoflocculation tests; staphylococci, streptococci, pneumococci; colon-typhoid-dysentery group (chapter 23); the corynebacterium, the clostridia; the mycobacteria; actinomyces; and mycopathogenic fungi. The Brucella group (chapter 32); cholera vibrio, spirochetes; the rikketsia group and the filtrable viruses are briefly and informatively presented. The instructive chapters on the parasitic protozoa (chapter 40) and on the bacteriology of water, milk and food (chapter 39) complete this compact well-written textbook. This book is recommended for medical students, public health officials, and those interested in the subject, including teachers in colleges and other institutions.

PULMONARY TUBERCULOSIS, PATHOLOGY, DIAGNOSIS, MANAGEMENT AND PREVENTION. Walter Pagel, M.D.; Pathologist, Central Middlesex County Hospital, London; F. A. H. Simmonds, M.A., M.D., D.P.H., Medical Director, Clare Hall County Hospital, Middlesex; N. Macdonald, M.B., M.R.C.P. Ed., Physician to the Chest Clinic, Redhill County Hospital, Middlesex, and L. Fatti,

F.R.C.S., Thoracic and Harefield County Hospital, Middlesex. Second edition, 720 pages. Oxford University Press, New York, London, 1948. Price $18.50.

Ten years ago the first edition of this excellent work appeared and since 1939 many helpful and life saving advances have been made in phthisiology and thoracic surgery. During this decade we have seen appearing on the scene streptomycin, anderomycin, terramycin, chloromycetin and aureomycin, and penicillin, dihydrostreptomycin, paraaminosalicylic acid, and other therapeutic remedies.

The surgical treatment of pulmonary tuberculosis and complications has now become well established.

This second edition covers the field of tuberculosis from every standpoint. It is a suitable and helpful addition to the other textbooks by Davidson, Judd, Pottenger, Rubin and Rich and others. In this work, the reader will find informatively and instructively presented "The Evolution of Tuberculosis in Man" (139 Pages).

Physical signs and symptoms; radiological examination of the chest and examination of the blood; forms of pulmonary tuberculosis; pleurisy with effusion; prognosis; modes of treatment including collapse therapy, chemotherapy, cavity drainage, and various other modes of treatment: lobectomy, pneumonectomy, thoracoscopy and adhesion section, pneumothorax, pneumoperitoneum and thoracoplasty, all receive concise, but adequate consideration. This work on pulmonary tuberculosis is highly recommended for all physicians to read and study. Thoracic surgeons, phthisiologists, clinicians, and general practitioners will find this book to be a source of much valuable and authoritative information.

DOCTOR AND PATIENT AND THE LAW. Louis J. Regan, M.D., LL.B., Professor of Legal Medicine, College of Medical Evangelists; Consulting Staff Hollywood Presbyterian Hospital, Los Angeles; Methodist Hospital of Southern California, Los Angeles; Physicians and Surgeons Hospital, Glendale, California; Member State Bar of California. Second edition, 545 pages. The C. V. Mosby Co., St. Louis, Mo., 1949. Price $10.00.

This book does not supplant the services of an attorney when the need arises! It is a source of considerable helpful information in preventing doctors from falling into legal pitfalls, which otherwise physicians would be entirely unprepared to foresee. Ofttimes ma'practice suits can be avoided, if the doctors would be better informed in the facts presented in this instructive volume.

The book should be especially helpful to surgeons and orthopedists and industrial physicians, and those engaged in emergency surgery and medicine. Since malpractice threats may arise at any time it is wise for busy surgeons and physicians to be informed as to many of these possible legal problems. Every medical library and clinic should have a copy.

SYNOPSIS OF HERNIA. Alfred H. Jason, M.D., Attending Surgeon, Adelphi Hospital; Director of Surgery, Brooklyn Hospital for the Aged; Instructor in Anatomy, New York Medical College. Illustration by Alfred Feinberg, New York City. 500 pages. Grune and Stratton, New York, 1949. Price $6.50.

This work is a condensed edition of the author's previous book (Blakiston, 1941) on hernia. This book, in a concise and clear manner, gives an informative presentation of the subject of hernia. The textbook covers the subject briefly and in an easily readable form.

"Classifications of Abdominal Hernias", "The Anterolateral Abdominal Wall", "Indirect Inguinal Hernia", "Cryptorchism"; the various types of inguinal hernia and the relations and components are among the topics considered.

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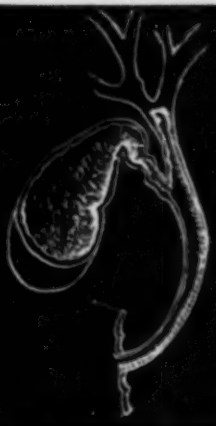

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1. Gastroenterology 3:56, 1944
2. Am. J. Roentgenol. 19:341, 1928
3. J. Lab. and Clin. Med. 18:1016, 1933
4. J. Lab. and Clin. Med. 19:567, 1934

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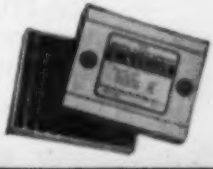

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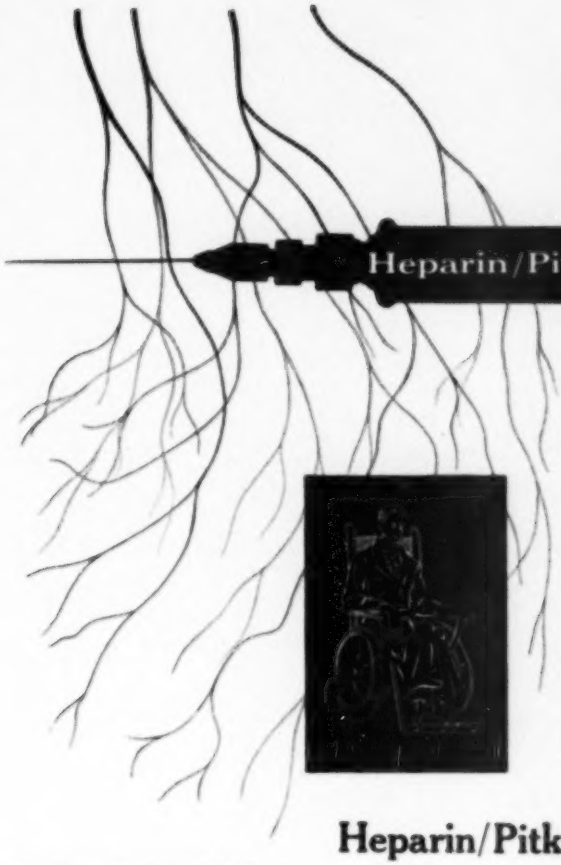

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References: (1) Loewe, L., Hirsch, E., Grayzel, D.M., and Kashdan, F.: Experimental Study of the Comparative Action of Heparin and Dicumarol on the *In Vitro* Clot, *J. Lab. Clin. Med.*, 33:721, 1948.
(2) Evans, J.A., and Dee, J.F.: Anticoagulant Treatment of Postoperative Venous Thrombosis and Pulmonary Embolism, *New Eng. J. M.*, 238:1, 1948.

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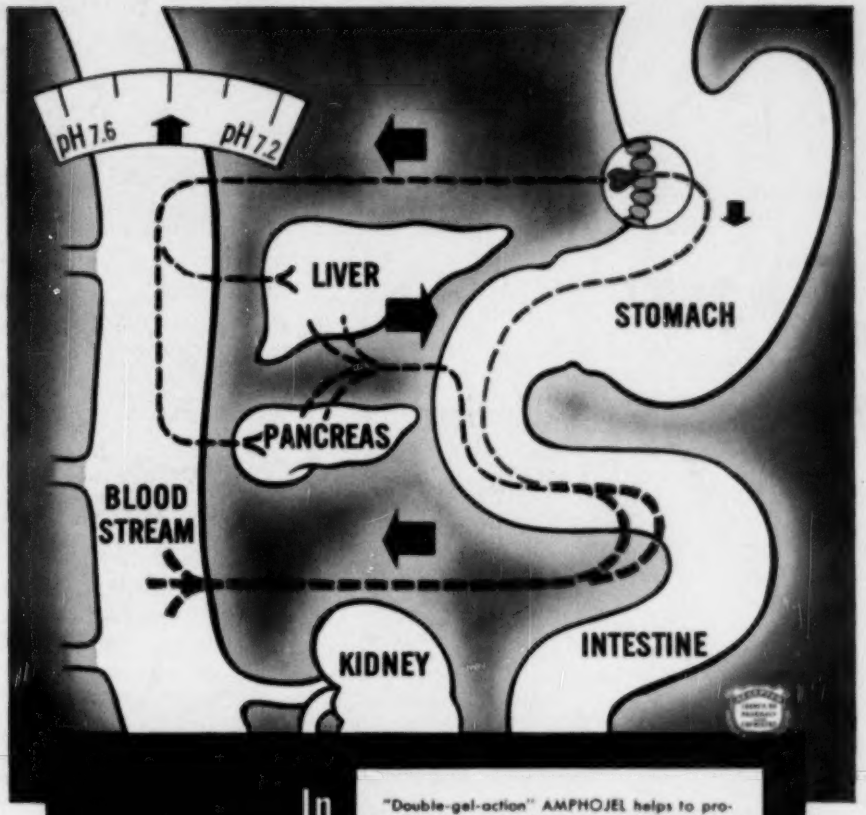

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